(26)

No. 05-608
Title: MedImmune, Inc., Petitioner
v.
Genentech, Inc., et al.
Docketed: November 15, 2005
Lower Ct: United States Court of Appeals for the Federal Circuit
Case Nos.: (04-1300, 04-1384)
Decision Date: October 18, 2005
Questions Presented

| ~~Date~~ | ~~~~~~~~Proceedings and Orders~~~~~~~~~~~~~~~~~~~~~~~~ |
|---|---|
| Nov 10 2005 | Petition for a writ of certiorari filed. (Response due December 15, 2005) |
| Dec 9 2005 | Order extending time to file response to petition to and including December 27, 2005. |
| Dec 27 2005 | Brief of respondents Genentech, Inc., et al. in opposition filed. |
| Jan 11 2006 | DISTRIBUTED for Conference of February 17, 2006. |
| Jan 12 2006 | Reply of petitioner MedImmune, Inc. filed. (Distributed) |
| Feb 21 2006 | Petition GRANTED. |
| Mar 10 2006 | Extension of time within which to file the joint appendix and petitioner's brief on the merits to and including May 8, 2006. |
| Apr 25 2006 | Consent to the filing of amicus briefs in support of either party received from counsel for the respondent Genentech only. |
| May 1 2006 | Further extension of time within which to file the joint appendix and petitioner's brief on the merits to and including May 15, 2006. |
| May 2 2006 | Letter from counsel for respondent City of Hope indicating that amicus consent will be addressed on an individual request basis. |
| May 12 2006 | Brief amici curiae of Three Intellectual Property Professors filed. |
| May 15 2006 | Further extension of time within which to file the joint appendix and petitioner's brief on the merits to and including May 17, 2006. |
| May 15 2006 | Brief amicus curiae of United States filed. |
| May 15 2006 | Brief amicus curiae of Generic Pharmaceutical Association filed. |
| May 15 2006 | Brief amicus curiae of Natural Resources Defense Council, Inc. filed. |
| May 15 2006 | Brief amicus curiae of Medtronic, Inc. filed. |
| May 15 2006 | Brief amicus curiae of Licensing Executives Society (U.S.A. & Canada), Inc. filed. |
| May 15 2006 | Brief of petitioner MedImmune, Inc. filed. |
| May 17 2006 | Joint appendix filed. Joint appendix in two volumes. |
| May 31 2006 | Extension of time within which to file respondents' briefs on the merits to and including July 26, 2006. |
| Jul 14 2006 | SET FOR ARGUMENT on Wednesday, October 4, 2006. |
| Jul 17 2006 | CIRCULATED. |
| Jul 18 2006 | Motion of the Solicitor General for leave to participate in oral argument as amicus curiae and for divided argument filed. |
| Jul 26 2006 | Brief of respondent Genentech, Inc. filed. (Distributed) |
| Jul 26 2006 | Brief amicus curiae of Boston Patent Law Association filed. (Distributed) |
| Jul 26 2006 | Brief amicus curiae of Pharmaceutical Research and Manufacturers of America filed. |

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|---|---|
| | (Distributed) |
| Jul 26 2006 | Brief of respondent City of Hope National Medical Center filed. (Distributed) |
| Jul 26 2006 | Brief amicus curiae of American Intellectual Property Law Association filed. (Distributed) |
| Jul 26 2006 | Brief amici curiae of Trustees of Columbia University in the City of New York, et al. filed. (Distributed) |
| Jul 26 2006 | Brief amici curiae of Qualcomm Incorporated and Interdigital Communications Corporation filed. (Distributed) |
| Jul 26 2006 | Brief amici curiae of Richard L. Donaldson, et al. filed. (Distributed) |
| Jul 26 2006 | Brief amici curiae of Professors John R. Allison, et al. filed. (Distributed) |
| Jul 26 2006 | Brief amicus curiae of New York Intellectual Property Law Association filed. (Distributed) |
| Jul 26 2006 | Brief amici curiae of Group of Law of Professors, Andrew Beckerman-Rodau, et al filed. (Distributed) |
| Jul 26 2006 | Brief amici curiae of 3M, General Electric, Proctor & Gamble, and E I.DuPont de Nemours filed. (Distributed) |
| Jul 26 2006 | Brief amicus curiae of American Bar Association filed. (Distributed). |
| Aug 3 2006 | Record received from U.S.C.A. for Federal Circuit. (1 box) |
| Aug 14 2006 | SET FOR ARGUMENT on Wednesday, October 4, 2006. |
| Aug 14 2006 | Application (06A172) to file petitioner's reply brief on the merits in excess of page limits, submitted to The Chief Justice. |
| Aug 16 2006 | Application (06A172) denied by The Chief Justice. |
| Aug 30 2006 | Reply of petitioner MedImmune, Inc. filed. (Distributed) |
| Sep 1 2006 | Motion of the Solicitor General for leave to participate in oral argument as amicus curiae and for divided argument GRANTED. |
| Sep 11 2006 | Record received from U.S.D.C. for the Central District of California. (3 boxes) |
| Oct 4 2006 | Argued. For petitioner: John G. Kester, Washington, D.C.; and Deanne E. Maynard, Assistant to the Solicitor General, Department of Justice, Washington, D.C. (for United States, as amicus curiae.) For respondents: Maureen E. Mahoney, Washington, D.C. |

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No. 05-608

IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,
*Petitioner*,

v.

GENENTECH, INC., *et al.*,
*Respondents*.

**Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## PETITION FOR A WRIT OF CERTIORARI

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## QUESTION PRESENTED

Does Article III's grant of jurisdiction of "all Cases . . . arising under . . . the Laws of the United States," implemented in the "actual controversy" requirement of the Declaratory Judgment Act, 28 U.S.C. § 2201(a), require a patent licensee to refuse to pay royalties and commit material breach of the license agreement before suing to declare the patent invalid, unenforceable or not infringed?

## LIST OF PARTIES

Petitioner was the only appellant in the court below. Respondents are Genentech, Inc., City of Hope, and Celltech R & D, Ltd., appellees in that court.

## LIST PURSUANT TO RULE 29.6

Petitioner is a publicly held corporation. No publicly held entity owns 10% or more of its stock.

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No. ___

MEDIMMUNE, INC.,

*Petitioner*,

v.

GENENTECH, INC., *et al.*,

*Respondents*.

**Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## PETITION FOR A WRIT OF CERTIORARI

Petitioner prays that a writ of certiorari issue to review the judgment of the United States Court of Appeals for the Federal Circuit entered in this case October 18, 2005.

## OPINIONS BELOW

The opinion of the United States District Court for the Central District of California is unreported and is reproduced in the Appendix at A. 21a.[1] The opinion of the United States Court of Appeals for the Federal Circuit is not yet reported and is reproduced at A. 1a.

[1] Citations to "A." are to the appendix to this petition. Citations to "C.A.A." are to the joint appendix filed in the Court of Appeals, and to "C." to the first amended complaint.

## JURISDICTION

The judgment of the Court of Appeals was entered October 18, 2005. This Court has jurisdiction pursuant to 28 U.S.C. § 1254(1).

## CONSTITUTIONAL AND STATUTORY PROVISIONS INVOLVED

Article III of the Constitution of the United States and 28 U.S.C. §§ 1331, 1338(a) and 2201(a) are reproduced at A. 32a.

## STATEMENT

### A. The License.

Petitioner, MedImmune, Inc., is a biotechnology company. It manufactures and markets Synagis®, the only drug in the United States indicated for prevention of potentially fatal respiratory tract infections caused by respiratory syncytial virus ("RSV") in infants. A. 21a. Synagis® is a monoclonal-antibody-based preventative agent.

Respondents Genentech, Inc., and City of Hope (hereinafter collectively "Genentech") hold two related patents directed broadly to methods of manufacturing monoclonal antibodies. The first, United States Patent No. 4,816,567, naming Shmuel Cabilly and others as inventors (the "Cabilly I patent"), issued March 28, 1989, and expires March 28, 2006. C.A.A. 638. The second, United States Patent No. 6,331,415, naming the same inventors (the "Cabilly II patent"), issued December 18, 2001, and following a settlement between Genentech and respondent Celltech—which petitioner challenged in this litigation—does not expire until 2018. C.A.A. 112. The Cabilly II patent includes claims that are copied from, and are virtually identical to, the claims of a 1989 patent assigned to respondent Celltech (U.S. Patent No. 4,816,397, the "Boss patent").[2] The invention claimed

[2] After the Boss patent issued in 1989, Genentech initiated a proceeding before the United States Patent and Trademark Office seeking a deter-

by the Boss and Cabilly II patents together will receive a total patent-protection period of 29 years. During this time, respondents may demand (and have demanded) licenses and royalty payments for what they describe as a fundamental technology for synthesizing monoclonal-antibody-based products. C. 25-26.

In 1997, a year prior to first marketing Synagis®, petitioner agreed to license a group of patents from Genentech. The license carried an obligation to pay royalties for the sale or marketing of any product covered by one of the patents, among which was the Cabilly I patent. A. 4a, 28a-29a, C. 5. Petitioner was a new company unable to afford extended litigation and unwilling to risk crippling infringement judgments, with possible consequences of injunction, treble damages and attorneys' fees. The licensed package also included, in addition to the Cabilly I patent, several patent applications that were pending, among them what became the Cabilly II patent, which at the time of the license was unissued and the scope of whose claims was uncertain.

In December 2001 the Cabilly II patent issued, and its claims were publicly disclosed for the first time. Less than a month later, Genentech notified petitioner of its "expectation

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mination that Genentech had been the first to invent the claimed subject matter. The PTO finally decided in Celltech's favor in 1998. Genentech then commenced litigation in the District Court, seeking to overturn the PTO's determination. The Boss patent was in force during this entire period, and was nearing the end of its 17-year term. But Genentech and Celltech then entered an agreement to settle the litigation. Celltech thereby reversed its position and agreed with Genentech that Genentech had been the first inventor; this removed the barrier that for ten years had prevented Genentech from obtaining the Cabilly II patent, and that patent (with a fresh 17-year term) issued soon afterwards. In return, Celltech received money payments from Genentech through 2006 (when the Boss patent was to expire), plus preferential access to the technology that was once covered by the Boss patent, and as a result of the agreement will be covered until 2018 by the Cabilly II patent.

that MedImmune will pay royalties on sales of its Synagis® antibody product" under the license based on the newly issued and disclosed Cabilly II patent. C. 26. Petitioner disputed that it had any obligation to pay royalties and requested Genentech to explain its "basis for believing that MedImmune's product would infringe any valid claim of the [Cabilly II] Patent such that royalties would be due." C. 27. Genentech ignored the request. In the meantime, fearing possible suit to prohibit its sale of Synagis®, which accounted for 80% of its revenues, petitioner began making the requested royalty payments, informing Genentech that "[s]uch payment . . . was made under protest and with reservation of all of our rights." *Id.*

The following year petitioner brought suit against respondents in the United States District Court for the Central District of California under the Declaratory Judgment Act, 28 U.S.C. § 2201(a), seeking a judgment that the Cabilly II patent—for a number of reasons including failure to disclose prior art and misleading the Patent and Trademark Office—was invalid and unenforceable and was not infringed by Synagis®.[3] A. 4a. To avoid the consequences of an injunction and the penalties of a possible finding of willful infringement, petitioner has continued to pay royalties under protest during the pendency of this litigation.

### B. District Court Decision.

The District Court (Pfaelzer, J.) in April 2004 dismissed petitioner's suit for lack of subject-matter jurisdiction. The District Court explained that it was bound to do so by a decision of the Federal Circuit announced the previous month, *Gen-Probe Inc.* v. *Vysis,* Inc., 359 F.3d 1376 (Fed. Cir.), *pet'n for cert. dismissed*, 125 S. Ct. 351 (2004) (No. 04-

[3] The complaint also claimed damages for antitrust violations and unfair competition under state and federal laws. The District Court dismissed those claims. See A. 22a.

260). That decision held that when a patent licensee had complied with, rather than breached, its royalty obligations, there was no "actual controversy" within the meaning of the Declaratory Judgment Act and the requirements of Article III of the Constitution. The District Court observed that it dismissed with reluctance, explaining:

> "In *Gen-Probe* the Federal Circuit determined that controversies over patent validity, enforcement, infringement would not be recognized while license agreements protected the licensee from suit for infringement.
>
> * * *
>
> "Even if *it has serious misgivings about the panel's conclusion*, this Court is not free to reconsider policy ramifications that *Gen-Probe* rejected. . . . Because *Gen-Probe* ruled that no subject matter jurisdiction exists under these facts, this Court must grant Genentech's Motion."

A. 29a, 31a (emphasis supplied). The District Court also pointed out that the Federal Circuit's new doctrine was a departure from the Circuit's previous constitutional understanding:

> "In the past, the 'actual controversy' requirement has not been interpreted as precluding a licensee from challenging a patent it licenses. *See C.R. Bard Inc. v. Schwartz*, 716 F.2d 874, 875 (Fed. Cir. 1983) ('[A] patent license need not be terminated before a patent licensee may bring a declaratory judgment action'); *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969) (holding that a license does not bar the licensee from challenging the validity of the patent).
>
> "In *Gen-Probe*, however, the Federal Circuit limited the ability of licensees to challenge the patents they license. The Court held that no actual controversy existed between a patentee and a licensee in good standing. *Gen-Probe* . . . (noting that the 'license, unless

> materially breached, obliterated any reasonable apprehension of a lawsuit based on the prior circumstances cited by the district court for jurisdiction.')."

A. 24a-25a. Accordingly, the court dismissed the declaratory-judgment claim and entered judgment for respondents. Petitioner appealed.

### C. Court of Appeals Decision.

The Federal Circuit, in an opinion by Judge Newman, joined by Judges Mayer and Clevenger, affirmed the dismissal, applying the jurisdictional rule announced in the *Gen-Probe* decision. According to that rule, to sue under Article III and the Declaratory Judgment Act "a licensee must, at a minimum, stop paying royalties (and thereby materially breach the agreement)." *Gen-Probe*, 359 F.3d at 1381. The Federal Circuit held that "the jurisdictional requirements of a declaratory judgment action are not met when royalties are fully paid to the licensor and there is no ground on which the licensor can cancel the license or sue for infringement." A. 6a. Without such a breach or termination, "there is no discretion to accept an action when there is no controversy of immediacy or reality because there is no reasonable apprehension of suit" when a licensee has not breached a license agreement. A. 8a.[4]

## REASONS FOR GRANTING THE WRIT

In an unprecedented reinterpretation of Article III and the Declaratory Judgment Act, the Federal Circuit has written into every patent license a "licensee estoppel" clause. The Federal Circuit has effectively ended actions by patent licen-

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[4] The Court of Appeals also affirmed the District Court's dismissal of petitioner's other claims. See n. 3, *supra*; A. 9a-17a. Judge Clevenger dissented from that part of the decision, concluding that the appeal of that dismissal should have been transferred to the United States Court of Appeals for the Ninth Circuit. A. 17a-20a.

sees to challenge patents, unless those licensees first place themselves in breach, and consequently in jeopardy of license termination, substantial liability and penalties. The Federal Circuit's new and absolute rule, laid down first in *Gen-Probe* last year, and followed undeviatingly once again here, is that any licensee

> "must, at a minimum, stop paying royalties (and thereby materially breach the agreement) before bringing suit to challenge the validity or scope of the licensed patent."

*Gen-Probe*, 359 F.3d at 1381. The Federal Circuit already has applied its new Article III rule, without any exception, in at least four decisions thus far,[5] and the district courts have obeyed.[6]

With particular respect to patents, as this Court explained its grant of certiorari to the Federal Circuit in *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83, 89 (1993):

> "Because the Federal Circuit has exclusive jurisdiction over appeals from all United States District Courts

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[5] See, in addition to *Gen-Probe* and the present decision, *MedImmune, Inc.* v. *Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005); *Metabolite Labs., Inc.* v. *Laboratory Corp. of America Holdings*, 370 F.3d 1354, 1369 (Fed. Cir. 2004) (vacating judgment because "in light of LabCorp's continuing royalty payments on the panel test, LabCorp cannot itself challenge the validity of a claim for which it continues to pay royalties"), *cert. granted*, 74 U.S.L. WEEK 3287 (2005) (No. 04-607). See also, applying the Federal Circuit interpretation of Article III outside the patent-license context, *Teva Pharmaceuticals USA, Inc.* v. *Pfizer, Inc.*, 395 F.3d 1324, *rehearing en banc denied*, 405 F.3d 990 (Fed. Cir.), *cert. denied*, 125 S. Ct. 1413 (2005) (No. 05-48).

[6] See *E.I. du Pont de Nemours & Co.* v. *Great Lakes Chem. Corp.*, 383 F. Supp. 2d 642 (D. Del. 2005) (applying *Gen-Probe* and dismissing declaratory judgment suit by licensee); *In re Columbia Univ. Patent Litig.*, 343 F. Supp 2d 35, 49 (D. Mass. 2004) ("If Biogen Idec MA and Genzyme pay the annual license fee, any possible case or controversy may be extinguished.").

> in patent litigation, the rule that it applied in this case . . . is a matter of special importance to the entire Nation."

So here also. Besides unduly constricting Article III, the decision is contrary to the policy of the patent laws themselves as declared in this Court's decision in *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969), which abolished the previous doctrine of licensee estoppel. And because the Federal Circuit is the sole appellate court for patent claims, its new doctrine now governs every United States patent licensee.

The Federal Circuit's decision ignores clear holdings of this Court, and what was heretofore the accepted understanding of the Declaratory Judgment Act in other Circuits, as applied also to copyright licenses, trademark licenses, and licensing contracts of every kind. If the Federal Circuit's constitutional rule is allowed to stand, MedImmune along with many other litigants, particularly small and innovative biotechnology companies, will be forced either to put themselves in material breach of license agreements (agreements often forced upon them) and thereby incur great financial risk, or to forgo any challenge to invalid or overreaching patent claims, even claims that issue after the license. Either way, they are denied the option of declaratory relief that Congress clearly intended to grant when it enacted the Declaratory Judgment Act in 1934.

## I. THE FEDERAL CIRCUIT'S NEW INTERPRETATION OF ARTICLE III AND THE DECLARATORY JUDGMENT ACT CONFLICTS WITH DECISIONS OF THIS COURT AND OTHER COURTS OF APPEALS.

### A. The Decision Is Contrary to This Court's Holdings Dating From *Aetna Life Ins. Co.* v. *Haworth*.

1. In its landmark holding in *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227 (1937), this Court through Chief Justice Hughes unanimously upheld the constitutionality under Article III of

the 1934 Declaratory Judgment Act, now 28 U.S.C. § 2201(a). This Court explained, in constitutional doctrine of general application, that

> "Where there is such a concrete case admitting of an immediate and definitive determination of the legal rights of the parties in an adversary proceeding upon the facts alleged, the judicial function may be appropriately exercised although the adjudication of the rights of the litigants may not require the award of process or the payment of damages."

300 U.S. at 241. This Court held that a dispute over the meaning of terms of insurance policies presented "a dispute . . . manifestly susceptible of judicial determination." *Id.* at 242.

Such is the case here. Just as in *Aetna*,

> "There is here a dispute between parties who face each other in an adversary proceeding. The dispute relates to legal rights and obligations arising from the contracts . . . . The dispute is definite and concrete, not hypothetical or abstract. Prior to this suit, the parties had taken adverse positions with respect to their existing obligations. . . . It calls, not for an advisory opinion upon a hypothetical basis, but for an adjudication of present right upon established facts."

300 U.S. at 242. The Cabilly II patent has been issued and is effective until 2018 and petitioner's product is on the market. Petitioner's claims of invalidity, unenforceability and noninfringement all are ripe for determination on a concrete record.

2. Soon after *Aetna* this Court specifically held that the Declaratory Judgment Act applied to a patent-license challenge. Pointing out the immediacy of the dispute, this Court explained that

> "certainly the requirements of case or controversy are met where payment of a claim is demanded as of right and where payment is made, but where the involuntary or coercive nature of the exaction preserves the right

> to recover the sums paid or to challenge the legality of the claim."

*Altvater* v. *Freeman*, 319 U.S. 359, 365 (1943). Further, this Court held:

> "It is said that so long as petitioners are paying royalties they are in no position to raise the issue of invalidity—the theory being that as licensees they are estopped to deny the validity of the patents and that, so long as they continue to pay royalties, there is only an academic, not a real controversy, between the parties. . . . The fact that *royalties were being paid* did not make this a 'difference or dispute of a hypothetical or abstract character.'"

*Id.* at 364 (emphasis supplied), quoting in part *Aetna*, 300 U.S. at 240.[7]

3. This Court has never deviated from those holdings. In fact, it has pointed out again the particular appropriateness of the Declaratory Judgment Act to patent litigation. Completely contrary to the Federal Circuit's rejection of jurisdiction here, this Court has held that

> "Merely the desire to avoid the threat of a 'scarecrow' patent, in Learned Hand's phrase, may therefore be sufficient to establish jurisdiction under the Declaratory Judgment Act."

*Cardinal Chemical*, 508 U.S. at 96 (footnote omitted), citing *Bresnick* v. *United States Vitamin Corp.*, 139 F.2d 239, 242 (2d Cir. 1943).

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[7] "As we said in *Fidelity National Bank* [*& Trust Co.* v. *Swope*, 274 U.S. 123, 132 (1927)], 'Naturalization proceedings, . . . suits to determine a matrimonial or other status; suits for instructions to a trustee or for the construction of a will . . . bills of interpleader so far as the shareholder is concerned . . . bills to quiet title where the plaintiff rests his claim on adverse possession . . . are familiar examples of judicial proceedings which result in an adjudication of the rights of litigants, although execution is not necessary . . . .'" *Nashville, C. & St. L. Ry.* v. *Wallace*, 288 U.S. 249, 263 (1933).

4. In adopting an absolute requirement that bars declaratory judgment suits and permits "no discretion," when "there is no defaulting licensee," A. 6a, 8a, the Federal Circuit has defied this Court's direction, reiterated in many cases, that

> "the question in each case is whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment."

*Maryland Cas. Co.* v. *Pacific Coal & Oil Co.*, 312 U.S. 270, 273 (1941). Instead, the Federal Circuit has attempted to distinguish the fundamental holdings of this Court on unpersuasive grounds. Faced with the *Aetna* decision, the Federal Circuit rejected it as inapplicable because, although *Aetna* "suggests that a litigant may sue to determine contract rights before a breach," that case "did not involve a declaratory judgment action instituted by a patent licensee in good standing." *Gen-Probe*, 359 F.3d at 1382. Faced with the *Altvater* decision, the Federal Circuit said that that case was inapplicable because the royalties called for by the license there were being paid pursuant to an injunction. *Id.* at 1381-82.

5. The question presented here is certainly "vital to the practice of patent law." *C.R. Bard, Inc.* v. *Schwartz*, 716 F.2d 874, 878 (Fed. Cir. 1983). But the Federal Circuit has rendered a decision reaching far beyond the patent context, and deep into Article III itself.[8] There is no way to confine its reasoning to a single subset of contracts, patent licenses. Contract disputes of all kinds were a primary focus of Congress when it enacted the Declaratory Judgment Act in

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[8] The "actual controversy" requirement of the Declaratory Judgment Act extends to the limits of the "Cases" or "Controversies" jurisdiction of Article III. *Aetna*, 300 U.S. at 239-40; *ACandS, Inc.* v. *Aetna Cas. & Surety Co.*, 666 F.2d 819, 822 (3d Cir. 1981).

1934: a party who disagrees about the meaning of a contract provision or the obligation imposed by it should not have to put itself in material breach before it can obtain an adjudication of its rights. Congress explained the Act's purpose to

> "enable[] parties in disputes over their rights over a contract, deed, lease, will, or any other written instrument to sue for a declaration of rights, *without breach of the contract* . . . ."

S. Rep. No. 1005, 73d Cong., 2d Sess. 2 (1934) (emphasis supplied). Referring to the previous legal situation—under which "it is often necessary to break a contract or lease, or act upon one's own interpretation of his rights when disputed"—the Senate Report explained that with the Declaratory Judgment Act "it is not necessary to bring about such social and economic waste and destruction in order to obtain a determination of one's rights." *Id.* In the words of a principal author of the Act, it was intended to allow a party disputing a contractual obligation an alternative to the choice of "risking disaster by acting on [its] own assumption or . . . not acting because of fear of consequences." E. BORCHARD, DECLARATORY JUDGMENTS 931 (2d ed. 1941). Its very purpose was to allow parties to litigate contract claims "without the necessity for prior breach." *Id.* at 932. *Accord, e.g.*, 10B C. WRIGHT, *et al.*, FEDERAL PRACTICE & PROCEDURE § 2751, at 457-58 (3d ed. 1998). Yet the Federal Circuit holds just the opposite: that a contracting party to a license agreement "must . . . materially breach the agreement . . . before bringing suit." *Gen-Probe*, 359 F.3d at 1381; see A. 6a ("there is no defaulting licensee and no possibility of suit").

A holding more contradictory to this Court's long-established construction and constitutional endorsement of the Declaratory Judgment Act, as well as of the patent laws, can scarcely be imagined. And the Federal Circuit, whatever its presumed technical competence in purely patent issues,

has no special expertise in construing Article III of the Constitution or the Declaratory Judgment Act.

### B. The Decision Is Contrary to Declaratory Judgment Holdings in Other Circuits.

The Federal Circuit's new line of Article III decisions, of which this is one, is completely at odds with how the Declaratory Judgment Act and Article III are construed in other circuits. Article III does not contain a special rule for patent licenses.

#### 1. *Licenses.*

Prior to the establishment of the Federal Circuit, several courts of appeals had held that patent licensees could bring declaratory judgment actions without first committing a breach of their license agreements. In *Precision Shooting Equip. Co.* v. *Allen*, 646 F.2d 313 (7th Cir.), *cert. denied*, 454 U.S. 964 (1981), the court pointed out the undesirability of forcing a licensee to "sit back and continue to wonder if it is justly paying royalties or merely paying a bribe to the patentee not to threaten him with business disruption and a possible damage suit if he terminates royalty payments." 646 F.2d at 318. It held that "[w]e see no need to force a party to take some additional act to deepen gray into black and to expand the potential of litigation resulting in further business disruption while we pretend in the meantime that there is no actual controversy." *Id.* at 318-19. It added that "[i]n determining . . . whether an 'actual controversy' exists in a particular circumstance, a determination which cannot be mechanically arrived at, the *Lear* rationale deserves to have some influence." *Id.* at 317.

Similarly the Second Circuit, in a frequently cited case, held that

> "Addressing the question whether a patent licensee must actually withhold royalty payments before he can

> challenge validity, we conclude—as have most courts who have considered the issue—that such repudiation of the licensing agreement should not be precondition to suit."

*Warner-Jenkinson Co.* v. *Allied Chem. Corp.*, 567 F.2d 184, 187 (2d Cir. 1977) (citing cases). *Accord*, *Société de Conditionnement* v. *Hunter Engineering Co.*, 655 F.2d 938, 943-44 (9th Cir. 1981) ("[d]eclaratory relief is 'indisputably appropriate' to patent cases"); *American Sterilizer Co.* v. *Sybron Corp.*, 526 F.2d 542, 546 (3d Cir. 1975) (termination of license not a precondition to declaratory suit by licensee).

The regional circuits since 1982 no longer pass upon this issue in the context of patent licenses. But those circuits do with regularity construe the Declaratory Judgment Act and Article III in the context of non-patent licenses, as well as other contracts. Although a patent licensee, the Federal Circuit here holds, is required by Article III to put itself in material breach before challenging its licensor, a copyright licensee, for instance, may seek a declaratory judgment without any such burden. The Ninth Circuit, applying patent-license principles to a copyright license, has held that a "licensee need not terminate its license agreement in order to maintain a federal declaratory action for copyright invalidity." *Hal Roach Studios, Inc.*, v. *Richard Feiner & Co.*, 896 F.2d 1543, 1556 n.23 (9th Cir. 1990). Non-patent licensees routinely are permitted to bring declaratory judgment actions without first committing breaches of the licenses. See *National Car Rental System, Inc.* v. *Computer Assocs. Int'l, Inc.*, 991 F.2d 426, 427-28 (8th Cir.), *cert. denied*, 510 U.S. 861 (1993); *S.O.S., Inc.* v. *Payday, Inc.*, 886 F.2d 1081, 1083 (9th Cir. 1989).

### 2. *Contracts Generally.*

The Federal Circuit decision here—holding that there must be a material breach of the license contract in order to present

a constitutional case or controversy under the Declaratory Judgment Act—is entirely in conflict with the numerous decisions in contract cases in other circuits that emphatically hold just the opposite. For many years, the other circuits have held that breach of contract is *not* necessary for jurisdiction of a declaratory-judgment action. *E.g.*, *Keener Oil & Gas Co.* v. *Consolidated Gas Utilities Corp.*, 190 F.2d 985, 989 (10th Cir. 1951) ("a party to a contract is not compelled to wait until he has committed an act which the other party asserts will constitute a breach, but may seek relief by declaratory judgment and have the controversy adjudicated in order that he may avoid the risk of damages or other untoward consequence"); *American Machine & Metals, Inc.* v. *De Bothezat Impeller Co.*, 166 F.2d 535, 536 (2d Cir. 1948) ("The very purpose of the declaratory judgment procedure is to prevent the accrual of . . . avoidable damages."). As the Fifth Circuit recently held, the Declaratory Judgment Act is designed "to avoid inequities which might result from a delay in assessing the parties' legal obligations," and "the court ought not require that those contingencies to [*sic*] have occurred at the time relief is sought." *Venator Group Specialty, Inc.* v. *Matthew/Muniot Family, LLC*, 322 F.3d 835, 840 (5th Cir. 2003) (declaratory judgment concerning obligations under commercial lease). For other examples, see:

> —*Doody* v. *Ameriquest Mortgage Co.*, 242 F.3d 286, 288 (5th Cir. 2001) ("The Declaratory Judgment Act exists to allow litigants to determine an actual controversy such as this one before the dispute grows into a contract violation . . . .").
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> —*NUCOR Corp.* v. *Aceros y Maquilas de Occidente, S.A.*, 28 F.3d 572, 577 (7th Cir. 1994) (Declaratory Judgment Act exists "to avoid accrual of avoidable damages to one not certain of his rights and to afford him an early adjudication, without waiting until his

adversary should see fit to begin suit, after damage had accrued.") (quotations omitted).

—*Continental Cas. Co.* v. *Coastal Sav. Bank*, 977 F.2d 734, 738 (2d Cir. 1992) ("[D]eclaratory judgment relief was intended to avoid precisely the accrual of avoidable damages to one not certain of his rights.") (quotation omitted).

—*United Food & Comm'l Workers Local No. 137* v. *Food Employers Council, Inc.*, 827 F.2d 519, 524 (9th Cir. 1987) (Declaratory Judgment Act "is intended to minimize the danger of avoidable loss and the unnecessary accrual of damages and to afford one threatened with liability an early adjudication without waiting until his adversary should see fit to begin an action after the damage has accrued," quoting 10A C. WRIGHT *et al.*, FEDERAL PRACTICE AND PROCEDURE § 2751, at 569-71 (2d ed. 1983)).

—*ACandS, Inc.* v. *Aetna Cas. & Surety Co.*, 666 F.2d 819, 823 (3d Cir. 1981) ("declaratory judgment relief was intended to avoid precisely the 'accrual of avoidable damages to one not certain of his rights'"), quoting *Dewey & Almy Chem. Co.* v. *American Anode, Inc.*, 137 F.2d 68, 69 (3d Cir.), *cert. denied*, 320 U.S. 761 (1943).

## II. THE DECISION FRUSTRATES THIS COURT'S DIRECTION IN *LEAR, INC.* V. *ADKINS.*

The Federal Circuit's decision also is at war with the policy enacted in the patent laws.

In *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969), this Court rejected the doctrine of "licensee estoppel" as "inconsistent with the aims of federal patent policy." 395 U.S. at 673. In *Lear* "[b]y 'unmuzzling' licensees, the Court sought to encourage the prompt adjudication of patent validity." *Nebraska Engineering Corp.* v. *Shivvers*, 557 F.2d 1257, 1259 (8th Cir. 1977), quoting in part *Atlas Chem. Industries, Inc.* v. *Moraine Prods.*, 509 F.2d 1, 6 (6th Cir. 1974).

*Lear* recognized that this Court since the Nineteenth Century has held that "[i]t is as important to the public that competition should not be repressed by worthless patents, as that the patentee of a really valuable invention should be protected in his monopoly . . . ." *Pope Mfg. Co.* v. *Gormully*, 144 U.S. 224, 234 (1892), quoted in *United States* v. *Glaxo Group Ltd.*, 410 U.S. 52, 58 (1973). And exactly a century after *Pope*, this Court reiterated in *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83, 100 (1993), "the importance to the public at large of resolving questions of patent validity." There is an

> "important public interest in permitting full and free competition in the use of ideas which are in reality a part of the public domain. Licensees may often be the only individuals with enough economic incentive to challenge the patentability of an inventor's discovery. If they are muzzled, the public may continually be required to pay tribute to would-be monopolists without need or justification."

*Lear*, 395 U.S. at 670. As this Court held, "We think it plain that the technical requirements of contract doctrine must give way before the demands of the public interest." *Id.*

Yet in addressing the *Lear* decision, the Federal Circuit observed—accurately—that "[i]n several instances, this court has declined to apply the *Lear* doctrine." *Gen-Probe*, 359 F.3d at 1381. At first the Federal Circuit had complied with *Lear*. In a 1983 decision it accordingly ruled that "[w]e hold that a patent licensee may bring a federal declaratory judgment action . . . without prior termination of the license." *C.R. Bard, Inc.* v. *Schwartz*, 716 F.2d 874, 882 (Fed. Cir. 1983). However, in *Diamond Scientific Co.* v. *Ambico, Inc.*, 848 F.2d 1220, 1224-25 (Fed. Cir.) *pet'n for cert. dismissed*, 487 U.S. 1265 (1988), the Federal Circuit ruled notwithstanding *Lear* that "despite the public policy encouraging people to challenge potentially invalid patents, there are still circum-

stances in which the equities of the contractual relationship between parties should deprive one party . . . of the right to bring that challenge." Then in 1997 the Federal Circuit characterized this Court's holding in *Lear* as sounding "tones that echo from a past era of skepticism over intellectual property principles." *Studiengesellschaft Kohle, m.b.H.* v. *Shell Oil Co.*, 112 F.3d 1561, 1567 (Fed. Cir.), *cert. denied*, 522 U.S. 996 (1997). The Federal Circuit candidly acknowledged that after *Lear* "this court nonetheless estopped the assignor from challenging the validity of the patent," and announced that

> "a licensee . . . cannot invoke the protection of the *Lear* doctrine until it (i) actually ceases payment of royalties . . . .

112 F.3d at 1567-68.

*Gen-Probe* and the present decision leave *Lear* virtually a dead letter in the Federal Circuit. In this case, following *Gen-Probe*, the Federal Circuit has resorted to misconstruction of Article III and the Declaratory Judgment Act to reject the patent policy recognized by this Court in *Lear* as something from a "past era." *Studiengesellschaft Kohle*, 112 F.3d at 1567.

The District Court here, reluctantly obeying the Federal Circuit, observed that what was being adopted was the Federal Circuit's own patent policy:

> "The *Gen-Probe* panel was concerned by the 'undesirable result' that licensors would bear more risk and be less likely to grant licenses if licensees were permitted to challenge the patents they license. . . . The panel was apparently more persuaded by this concern than by the potential that invalid or unenforceable patents will stand because licensees will be too risk-averse to challenge them."

A. 29a-30a. The District Court also pointed out that this "forces licensees to take a tremendous risk to challenge a

patent, one that some with valid claims will likely be unwilling to take." A. 30a.

Article III does not exist to promote particular substantive policies, but rather sets the parameters of the federal judicial power. Jurisdiction under Article III is not precluded "so long as the case retains the essentials of an adversary proceeding, involving a real, not a hypothetical, controversy, which is finally determined by the judgment below." *Nashville, C. & St. L. Ry.* v. *Wallace*, 288 U.S. 249, 264 (1933). The Declaratory Judgment Act tracks fully the scope of Article III. *Aetna*, 300 U.S. at 239-40; *ACandS*, 666 F.2d at 822. Nevertheless, as the Federal Circuit recognized, A. 7a, its interpretation of Article III's jurisdictional grant relies on considerations of patent policy it deems persuasive. See A. 7a; see also *Gen-Probe*, 359 F.3d at 1382.

Moreover, even if it were appropriate to reshape Article III in light of such substantive considerations, the Federal Circuit has adopted a policy at odds with the policy of the patent laws as declared by this Court, see *Lear*, *supra*, and failed to recognize the difficulties its new holding creates.

## III. THE DECISION PARTICULARLY INHIBITS THE INTRODUCTION OF NEW MEDICAL DRUGS AND TREATMENTS.

Disallowing licensee challenges to patent validity, as this Court has observed, has an effect "particularly severe in the many scientific fields in which invention is proceeding at a rapid rate." *Lear*, 395 U.S. at 673. It is common in the essential and fast-growing biotechnology industry to license a package of patents, as was done here, in a single license. By prohibiting declaratory challenges to patents unless royalty payments are stopped, the present decision will further encourage patent holders to bundle unrelated "bad" patents with "good" ones, betting that licensees will not risk losing the coverage of the valid patents in order to challenge the doubt-

ful ones. Also, patents licensed under agreements typically are defined to include "continuations, continuations-in-part, divisionals" and the like. Patent license agreements typically permit the licensor to terminate for any material breach, and treat such a breach as unallocated and applicable to the entire license, so that a licensee faced with a newly-issued invalid patent will be unable to challenge it without risking breach of the entire license and all the patents it includes.

This case presents a striking, but unfortunately all too common, example of how patent-holders can use the threat of litigation to assert claims and exact tributes to which they are not entitled. Here the license for respondent's patent package included an application that, upon its issuance as a patent and publication of its claims, petitioner believed to be invalid and unenforceable.

Such invalid patent claims carry a significant social cost. They inhibit innovation. This Court in *Lear* recognized the "important public interest," 395 U.S. at 670, in challenges to patents. The wisdom of that concern is reflected in the conclusion of recent research that when patents are challenged in litigation, they are held invalid 46% of the time. J. Allison & M. Lemley, *Empirical Evidence on the Validity of Litigated Patents*, 26 AM. INTELL. PROP. L.A.Q.J. 185, 205-06 (1998).

Petitioner's attempt to challenge the very broad patent claims Genentech asserted here on basic and important categories of drugs was grounded. Petitioner alleged, for example, that in order to obtain the Cabilly II patent, Genentech had intentionally withheld evidence concerning material prior art from the Patent and Trademark Office, and had obtained a patent monopoly on claims far beyond what experimental submission could support. C. 19-24. Yet in spite of the statutory policy that "competition should not be repressed by worthless patents," *Pope, supra; Glaxo Group, supra*, the Federal Circuit here has effectively enacted just the opposite policy, citing its own conclusion that challenges like peti-

tioner's would produce "undesirable results." *Gen-Probe*, 359 F.3d at 1382. The Court of Appeals was persuaded that "[a]llowing this action to proceed would effectively defeat those contractual covenants and discourage patentees from granting licenses." *Id.*[9] But this Court in *Lear* concluded that "contract doctrine must give way before the demands of the public interest." 395 U.S. at 670. And even if the questionable policy judgment embodied in the present decision were correct, it was not the Federal Circuit's to make, and certainly not by altering the meaning of Article III and the Declaratory Judgment Act.

That the Federal Circuit has nearly exclusive appellate jurisdiction nationally over appeals in cases involving patents is all the more reason not to allow its Article III and patent policy embodied in this decision, so contrary to the holdings of this Court and the reasoning of other circuits—and so powerful in steering the course of American industry—to stand unreviewed. See *Cardinal Chem. Co.*, 508 U.S. at 89. *Cf. Laboratory Corp. of America Holdings* v. *Metabolite Labs., Inc.*, 74 U.S.L. WEEK 3287 (2005) (No. 04-607) (granting certiorari to resolve asserted conflict on patent issue within the Federal Circuit).

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[9] By contrast, the Seventh Circuit in *Precision Shooting* was impressed by the undesirability of forcing a licensee to "wonder if it is justly paying royalties or merely paying a bribe." 646 F.2d at 318.

## CONCLUSION

For the reasons stated, certiorari should be granted.

Respectfully submitted,

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November 10, 2005

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# APPENDIX

**APPENDIX A**

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

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04-1300, -1384

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MEDIMMUNE, INC.,
*Plaintiff-Appellant,*

v.

GENENTECH, INC.,
*Defendant-Appellee,*

and

CITY OF HOPE,
*Defendant-Appellee,*

and

CELLTECH R&D, LTD.,
*Defendant-Appellee.*

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DECIDED: October 18, 2005

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Before NEWMAN, MAYER, and CLEVENGER, *Circuit Judges.*

Opinion for the court filed by *Circuit Judge* NEWMAN. Dissenting in part opinion filed by *Circuit Judge* CLEVENGER.

NEWMAN, *Circuit Judge.*

MedImmune, Inc., a licensee in good standing under a patent owned by Genentech, Inc. and City of Hope (collectively "Genentech"), seeks by declaratory action to challenge the validity and enforceability of the licensed patent on various

grounds flowing from the settlement of a patent interference between Genentech and Celltech R&D, Ltd. The United States District Court for the Central District of California held that because MedImmune continues to comply fully with the license terms, leaving no possibility of infringement suit or license cancellation by Genentech, there is no "case of actual controversy" as required by the Declaratory Judgment Act, 28 U.S.C. §2201. The district court also dismissed MedImmune's antitrust and unfair competition counts. We affirm the judgment.[1]

## BACKGROUND

The patented technology relates to the use of cell cultures to manufacture human antibodies. Genentech, Inc. and the City of Hope are the owners of United States Patent No. 4,816,567 (the Cabilly I patent) filed on April 8, 1983, and Patent No. 6,331,415 (the Cabilly II patent), a continuation of Cabilly I, filed on June 10, 1988. Celltech owns United States Patent No. 4,816,397 (the Boss patent), having a British priority date of March 25, 1983. In accordance with 35 U.S.C. §135 the United States Patent and Trademark Office (PTO) declared an interference between the Boss patent and the Cabilly II application. The PTO interference proceedings consumed seven and a half years. The Board of Patent Appeals and Interferences decided priority in favor of the senior party Boss, holding that Cabilly had not established an actual reduction to practice before the Boss patent's British priority date. *Cabilly v. Boss*, 55 USPQ2d 1238 (Bd. Pat. App. & Int. 1988).

Genentech then filed a civil action in the United States District Court for the Northern District of California, in accordance with 35 U.S.C. §146. After various proceedings, the district court concluded that disputed facts concerning con-

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[1] *MedImmune, Inc. v. Genentech, Inc.*, CV 03-2567 (C.D. Cal. Jan. 14, 2004; February 18, 2004; Mar. 15, 2004; April 29, 2004).

ception and reduction to practice required trial and, referring to the complexity of the science, stated that "[t]here appears to be a dispute amongst highly educated and apparently well-qualified experts" as to the interpretation and probative value of the evidence. The court urged Genentech and Celltech to resolve the issue of priority with the aid of mediation. Genentech and Celltech retained a mediation service, and a retired judge served as mediator. A settlement agreement was duly reached, whereby Genentech and Celltech agreed that the Cabilly II application was entitled to priority as against the Boss patent, based in part on new evidence of the content of a draft patent application during the period leading to filing of the Genentech application. Genentech and Celltech also entered into a cross-license agreement that included a formula for sharing of royalties. The district court entered judgment on the parties' resolution of the issue of priority, and directed the PTO to vacate its prior decision, revoke the Boss patent, and issue a patent on the Cabilly II application. *Genentech, Inc. v. Celltech R&D, Ltd.*, No. 3:98cv03929 (N.D. Cal. March 16, 2001).

Genentech and Celltech jointly presented the district court's judgment to the PTO, with a petition requesting that the PTO cancel the Boss patent and issue a patent on the Cabilly II application. The Board entered an order that Cabilly was the prior inventor, but did not precisely follow the requested procedure. The Board stated that the Boss patent was cancelled by operation of law when the district court's judgment became final and was not appealed, and that no further action by the PTO was required. The Board also observed that an Information Disclosure Statement filed by Genentech in 1991 had not been acted upon, and returned the Cabilly II application to the patent examiner for review of any "ground not involved in judicial review." Genentech then cited a large number of additional references to the examiner, and provided various documents from the record of the §146 action. After further examination the Cabilly II patent was issued on

December 18, 2001, eleven years after the inception of the interference.

MedImmune had since 1997 been licensed by Genentech under the Cabilly I patent and, by the terms of that agreement, received a license under the Cabilly II patent. In addition, MedImmune had since 1998 been licensed by Celltech under the Boss patent. After issuance of Cabilly II, Genentech advised MedImmune that a MedImmune product, brand name Synagis®, was covered by Cabilly II and subject to royalties in accordance with the license terms. MedImmune objected, and filed this declaratory judgment action in the Central District of California, requesting a declaration that the Cabilly II patent is invalid or unenforceable. MedImmune paid and continues to pay the license royalties to Genentech, relying on precedent such as *Cordis Corp. v. Medtronic, Inc.*, 780 F.2d 991 (Fed. Cir. 1985) for the holding that the licensor cannot terminate the license if the royalties are paid to the licensor and the license agreement is not otherwise breached. The district court, applying *Gen-Probe, Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir. 2004), dismissed the suit as non-justiciable under the Declaratory Judgment Act.

## DISCUSSION

### I

The district court held that MedImmune, as a licensee in good standing and not in reasonable apprehension of suit, cannot bring a declaratory action to challenge the patent under which it is licensed. MedImmune concedes that it is free of apprehension of suit, stating that the reason it is paying the royalties is to avoid the risk and possible consequences of a successful infringement suit by Genentech. However, MedImmune argues that under *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969) it has the absolute right to challenge the validity or enforceability of the patent, whether or not it breaches the license and whether or not it can be sued by the patentee.

MedImmune states that the *Gen-Probe* decision improperly resurrected the licensee estoppel that was abolished in *Lear*, and should be overturned.[2]

Genentech responds that this is not a question of licensee estoppel under *Lear*, but a question of Article III jurisdiction under the Declaratory Judgment Act. Unlike the situation in *Lear*, MedImmune is paying the license royalties; and unlike the situation in *Lear*, Genentech has no ground on which to cancel the license or otherwise bring suit affecting the licensed subject matter. In *Lear* the licensee stopped paying royalties and the patentee sued for royalties; there was clearly a justiciable controversy, and that aspect was not an issue in *Lear*. In contrast, in *Gen-Probe* the licensee was complying fully with the license terms and could not be sued by the patentee. Similarly, MedImmune is complying fully with the license terms and cannot be sued by the patentee.

MedImmune argues that although it has no reasonable apprehension of suit, it meets the requirements of the Declaratory Judgment Act because if it stopped paying royalties it could be sued. MedImmune states that the Cabilly II patent is subject to challenge on several grounds, and that it should not be shielded from such challenge. MedImmune also distinguishes its situation from that in *Gen-Probe* on the ground that the licensee in *Gen-Probe* negotiated for a license and then filed suit to invalidate the licensed patent, having secured its right to operate and the royalty terms should it lose the suit; MedImmune points out that it already had a license to Cabilly II under its license to Cabilly I and that the royalty rate was already set.

The district court was not persuaded by these distinctions, and we agree that they do not create a justiciable controversy.

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[2] Panels of the Federal Circuit are bound by prior decisions of this court unless overturned by the court *en banc*. *See, e.g., Sacco v. Dep't of Justice*, 317 F.3d 1384, 1386 (Fed. Cir. 2003).

Unlike the facts in *Lear*, where the licensee ceased payment and disavowed the license obligation, in *Gen-Probe*, as for MedImmune, breach was assiduously avoided. Thus this case does not raise the question of whether patent invalidity is available as a defense to suit against a defaulting licensee—the licensee estoppel that was laid to rest in *Lear*—for there is no defaulting licensee and no possibility of suit.

Precedent follows this pattern. For example, in *Intermedics Infusaid, Inc. v. Regents of University of Minnesota*, 804 F.2d 129, 131 (Fed. Cir. 1986), where suit was ongoing in state court for royalties under a license agreement, the court held that a federal declaratory judgment action challenging validity was properly stayed. In *Cordis v. Medtronic*, 780 F.2d at 995, the court held that to avoid breach during litigation the royalties were required to be paid to the licensor, not into escrow. In *C.R. Bard, Inc. v. Schwartz*, 716 F.2d 874, 875-76 (Fed. Cir. 1983) the licensee had stopped paying royalties and the licensor was suing for their recovery in state court but had not terminated the license; this court held that this material breach generated an actual controversy for purposes of the federal declaratory judgment challenge to validity. The decision in *Gen-Probe* is in accord with this precedent, in holding that the jurisdictional requirements of a declaratory action are not met when royalties are fully paid to the licensor and there is no ground on which the licensor can cancel the license or sue for infringement.

MedImmune stresses the public policy served by permitting it to attack the Genentech patent, and argues that estoppel has been eliminated in the fields of intellectual property as a matter of public policy. However, the issue here is not one of estoppel, but of availability of the declaratory judgment procedure. The purpose of that procedure is to "accommodate[] the practical situation wherein the interest of one side to the dispute may be served by delay in taking legal action," *BP Chemicals Ltd. v. Union Carbide Corp.*, 4 F.3d 975, 977

(Fed. Cir. 1993), by permitting the other side to initiate legal action. *See also, e.g., EMC Corp. v. Norand Corp.*, 89 F.3d 807, 814-15 (Fed. Cir. 1996); *Arrowhead Industrial Water, Inc. v. Ecolochem. Inc.*, 846 F.2d 731, 734-35 (Fed. Cir. 1988). The court in *Gen-Probe* discussed the inequity when the patent owner, having contracted away its right to sue, is in continuing risk of attack on the patent whenever the licensee chooses—for example, if the product achieves commercial success—while the licensee can preserve its license and royalty rate if the attack fails. This imbalance distorts the equalizing principles that underlie the Declaratory Judgment Act.

MedImmune states that cases from other circuits hold that a licensee need not terminate its license in order to acquire declaratory standing. However, in each of the cited cases there was an additional factor, such as money owed on the contract, or the plaintiff or its indemnitee had been threatened with suit, or there was a change in circumstances which affected performance of the contract, meeting the constitutional and statutory requirements that there must be an actual controversy in order to invoke judicial authority. Contrary to MedImmune's argument, the fact that the licensed subject matter is intellectual property does not create a policy-driven exception to these requirements.

In *MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005) the court adhered to *Gen-Probe* in circumstances, like those at bar, where MedImmune had secured a license and then sued to invalidate the licensed patent. The court explained that: "To keep watch over the subtle line between an 'abstract question' and 'a controversy contemplated by the Declaratory Judgment Act' an inquiry has been formulated [whereby] there must be both (1) a reasonable apprehension on the part of the declaratory judgment plaintiff that it will face an infringement suit, and (2) present activity by the declaratory judgment plaintiff which could constitute infringement . . . ." This synthesis of the totality-of-the-

circumstances test for determining whether there is a justiciable controversy is pragmatically useful. *See BP Chemicals*, 4 F.3d at 978 ("The purpose of the two-part test is to determine whether the need for judicial attention is real and immediate, or is prospective and uncertain of occurrence.")

Licensor and licensee always have "adverse legal interests," *Aetna Life Inc. Co. v. Haworth*, 300 U.S. 227, 241 (1937), but that relationship alone does not create a justiciable controversy. The Declaratory Judgment Act requires a "definite and concrete controversy," *id.* at 240, of "sufficient immediacy and reality," *Maryland Cas. Co. v. Pacific Coal & Oil Co.*, 312 U.S. 270, 273 (1941), to warrant judicial intervention. MedImmune avoided and continues to avoid such a situation, by avoiding breach and avoiding apprehension of suit. Thus although courts have discretion in deciding whether to accept a declaratory action when the constitutional and statutory requirements are met, there is no discretion to accept an action when there is no controversy of immediacy or reality because there is no reasonable apprehension of suit.

MedImmune directs us to the reference to "scarecrow" patents in *Cardinal Chemical Co. v. Morton International, Inc.*, 508 U.S. 83, 96 (1993). That case concerned the appellate obligation to review a district court's decision concerning patent validity, lest an invalid patent be revived. In *Cardinal Chemical* the trial court had decided the issues of infringement and validity, and the Court held that the Federal Circuit has the power to review both issues on appeal, and should do so, even when the patent is held not infringed. *Cardinal Chemical* was an infringement suit, not a declaratory action. As commented in *Super Sack Manufacturing Corp. v. Chase Packaging Corp.*, 57 F.3d 1054, 1060 (Fed. Cir. 1995), "nothing in *Cardinal* undermines our decisions on declaratory justiciability at the trial court level." The present case is unaffected by *Cardinal Chemical.*

The district court did not err in holding that MedImmune, since under no threat or apprehension of suit, did not have standing to bring a declaratory challenge to the Cabilly II patent.

II

MedImmune also argues that the interference settlement between Genentech and Celltech was collusive and fraudulent, and that this provides an independent basis for standing to attack the Cabilly II patent, whether or not the case or controversy requirement of the Declaratory Judgment Act is met. The district court held that the joint action of Genentech and Celltech was protected by the *Noerr-Pennington* doctrine.

MedImmune states that Genentech and Celltech violated federal and state antitrust laws, citing sections 1 and 2 of the Sherman Act (15 U.S.C. §§1,2), and the California antitrust and unfair competition statutes, Cal. Bus. & Prof. Code §16720 and §17200 et seq. MedImmune points out that the Cabilly II patent expires significantly later than the Boss patent (because of the interference delays), and argues that extension of control of the invention was the motivation for the agreement to award priority to Cabilly II. MedImmune also states that Celltech's Boss patent would have retained priority based on its British filing date if the district court had excluded the newly presented evidence of the draft Cabilly patent application. MedImmune states that this evidence, since not before the PTO, should not have been permitted in the district court. However, new evidence may be presented in §146 proceedings, *see* 35 U.S.C. §146 ("without prejudice to the right of the parties to take further testimony"). *See also Abbott Labs. v. Brennan*, 952 F.2d 1346, 1348 (Fed. Cir. 1991).

MedImmune refers to *United States v. Singer Mfg. Co.*, 374 U.S. 174 (1963), wherein the Court found Sherman Act violation based on interference settlements and other agreements among domestic sewing machine manufacturers for the

purpose of excluding Japanese competitors from the United States market. MedImmune argues that settling interferences "at least in part, to prevent an open fight over validity" of itself violates the Sherman Act, quoting the concurring opinion in *Singer*, 374 U.S. at 199 (White, J., concurring). The settlement of disputes such as priority in patent interferences is not a presumptive violation of antitrust law; such violation requires a showing of market power and other antitrust predicates. A patent does not of itself confer market power or a presumption thereof for purposes of the antitrust laws. *See C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1368 (Fed. Cir. 1998) ("It is not presumed that the patent-based right to exclude necessarily establishes market power in antitrust terms."); *Abbott Labs.*, 952 F.2d. 396 F.3d 1342, 1348 (Fed. Cir. 2003) ("the Supreme Court has held that there is a presumption of market power in patent tying cases"), *cert. granted*, 125 S. Ct. 2937 (June 20, 2005); Herbert Hovenkamp, at 1354 (Fed. Cir. 1991) ("A patent does not of itself establish a presumption of market power in the antitrust sense."); *American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350, 1367 (Fed. Cir. 1984) ("patent rights are not legal monopolies in the antitrust sense of the word"); *Jefferson Parish Hosp. Dist. No. 2 v. Hyde*, 466 U.S. 2, 18 (1984) ("any inquiry into the validity of a tying arrangement must focus on the market or markets in which the two products are sold, for that is where the anticompetitive forcing has its impact"); *In re Independent Service Organizations Antitrust Litigation*, 203 F.3d 1322, 1329 (Fed. Cir. 2000) ("patent alone does not demonstrate market power"); *Independent Ink, Inc. v. Illinois Tool Works, Inc.*, 396 F.3d 1342, 1348 (Fed. Cir. 2003) ("the Supreme Court has held that there is a presumption of market power in patent tying cases"), *cert. granted*, 125 S. Ct. 2937 (June 20, 2005); Herbert Hovenkamp, *Federal Antitrust Policy: The Law of Competition and its Practice* §10.3 (3d ed. 2005) ("most patents confer absolutely no market power on their owners").

The antitrust posture that MedImmune urges for patent interferences can discourage if not prevent settlements, placing unnecessary burdens on the courts and the PTO. Priority determinations may raise complex questions of law and scientific fact, and the delays in their resolution by the PTO are notorious; settlement can, as here, expedite resolution of difficult issues. The per se or presumptive illegality urged by MedImmune for interference settlements is contrary to both precedent and policy, as recorded in the *Antitrust Guidelines for the Licensing of Intellectual Property*, 4 Trade. Reg. Rep. (CCH) ¶13,132, §2.2 (1995).

III

MedImmune also argues that Genentech and Celltech colluded in the joint submission of their settlement agreement to the district court, and again in their joint submission of the court's judgment order to the Patent and Trademark Office with the request that the Boss patent be cancelled and the Cabilly II application be granted. The district court dismissed these claims, holding that petitions for governmental action are immune under the *Noerr-Pennington* doctrine that permits collaboration among competitors to petition the government to take an action that may restrain competition, without incurring antitrust liability by the act of collaborating. *See Eastern Railroad Presidents Conference v. Noerr Motor Freight, Inc.*, 365 U.S. 127, 136 (1961) (it is permissible for railroads to act in concert to petition the legislature to take an action that creates a restraint of trade or a monopoly); *United Mine Workers of America v. Pennington*, 381 U.S. 657, 671 (1965) (it is permissible for a combination of workers and their employers to petition the Secretary of Labor to take an action that adversely affects competitors). In *California Motor Transport v. Trucking Unlimited*, 404 U.S. 508 (1972) this immunity was extended to petitions to the courts "respecting resolution of [petitioners'] business and economic interests vis-a-vis their competitors." *Id.* at 511.

A joint communication to a court of the terms of settlement of a matter before the court, and a joint petition to the PTO to implement the court's judgment, are not actions that would be prohibited or tainted absent immunization by *Noerr-Pennington*; thus it was unnecessary for the district court to have relied on *Noerr-Pennington* immunity. Genentech and Celltech, the parties to the litigation in the district court, were obligated to bring their settlement to the court, and to bring the court's judgment to the PTO. Although MedImmune argues that the settlement "contains misrepresentations," the putative misrepresentation was by "representing [to the district court] that Genentech was instead entitled to priority." MedImmune Br. at 48. The district court properly rejected this theory, observing that disputed issues from the underlying litigation cannot be recast as misrepresentations, citing *Kottle v. Northwest Kidney Centers*, 146 F.3d 1056, 1063 (9th Cir. 1998). MedImmune's disagreement with the result of the priority settlement does not convert it into a presumptive violation of the antitrust laws, or grant MedImmune standing to require judicial review of the evidence and the conclusion reached in the settlement.

The ensuing filing of the judgment in the PTO is set by statute, and the joint filing by the parties to the judgment does not require *Noerr-Pennington* protection. *See* 35 U.S.C. §146 (filing in the Patent and Trademark Office of a certified copy of the judgment). The joint request of the litigants that the PTO implement the judgment is not a prohibited collusion.

## IV

MedImmune also argues that antitrust violation arose in Genentech's prosecution of the Cabilly II application after it was returned to ex parte examination. MedImmune states that the additional references that Genentech brought to the examiner's attention should have been presented earlier, that Genentech did not tell the examiner about certain patents under which Genentech was licensed, that Genentech made

inconsistent arguments from those it made in an opposition to the Boss patent in the European Patent Office, that Genentech cited so many references that the most important were "buried," and that Genentech did not tell the examiner about challenges to Cabilly II that Celltech had raised during the interference proceeding. Thus MedImmune states that the prosecution was fraudulent, and that enforcement of a fraudulently obtained patent violates the antitrust laws in terms of *Walker Process Equipment, Inc. v. Food Machinery & Chemical Corp.*, 382 U.S. 172 (1965).

The district court held that "this argument fails because in its Amended Complaint, MedImmune does not plead fraud" and that "MedImmune's *Walker Process* theory is not supported in the pleadings." Like all fraud-based claims, *Walker* Process allegations are subject to the pleading requirements of Fed. R. Civ. P. 9(b). *See Vess v. Ciba-Geigy Corp. USA*, 317 F.3d 1097, 1103-04 (9th Cir. 2003) (claims that are "grounded in fraud" or that "sound in fraud" are subject to Rule 9(b)). MedImmune's counsel emphasized, on questioning by the district court, that he was not charging fraud. The district court correctly held that the pleadings, which charged Genentech with inequitable conduct, not fraud, fell short of alleging a *Walker Process* antitrust violation.

Genentech describes MedImmune's approach as tactical. Whatever its basis, after the grant of summary judgment MedImmune sought to amend its pleadings by filing a Second Amended Complaint, to add the charge of fraud on the grounds that were previously designated as inequitable conduct. The district court denied leave to amend, referring to the litigation history and describing the proposed amendments as "prejudicial and futile." The Ninth Circuit reviews denials of leave to amend under an abuse of discretion standard. *Bowles v. Reade*, 198 F.3d 752, 757 (9th Cir. 1999).[3] MedImmune

[3] Leave to amend is a procedural matter not unique to patent law, and we apply the law of the regional circuit to review denial of leave to amend.

has provided no reasonable basis for deeming this ruling an abuse of the district court's sound discretion. In *Royal Insurance Co. of America v. Southwest Marine*, 194 F.3d 1009, 1017 (9th Cir. 1999) the court affirmed denial of leave to amend when the motion was made after the grant of summary judgment. Although the parties have in their briefs discussed at some length the prosecution aspects challenged by MedImmune, we discern no error in the district court's determination that MedImmune was without a reasonable likelihood of supporting a claim of antitrust violation, and that the proposed redesignation of prosecution issues as constituting fraud was tardy and prejudicial.

In addition, MedImmune's charge of fraud during ex parte patent examination does not establish standing to bring a declaratory action to invalidate a patent not involved in a case or controversy between the parties. The standards for determining jurisdiction in a declaratory judgment action of patent invalidity do not change when the declaration raises a *Walker Process* claim. *See Unitherm Food Sys., Inc. v. Swift-Eckrich, Inc.*, 375 F.3d 1341, 1357-58 (Fed. Cir. 2004) (as for other declaratory challenges to patent validity, reasonable apprehension of suit is a prerequisite for standing to bring an antitrust challenge to the patent prosecution). A person not under reasonable apprehension of suit cannot overcome the absence of declaratory standing simply by challenging the patent prosecution and asserting fraud. There is neither statutory nor precedential authority for collateral attack on patent examination procedures, by a person who does not meet the requirements of declaratory judgment standing.

MedImmune also states that it should have been permitted to file the Second Amended Complaint after the summary judgment, to add a charge of fraud in the tardy filing of the

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*See Ferguson Beauregard/Logic Controls Div. of Dover Resources, Inc. v. Mega Sys. LLC*, 350 F.3d 1327, 1342 (Fed. Cir. 2003).

interference settlement agreement. The PTO accepted the filing, as authorized by 35 U.S.C. §135(c). MedImmune challenges the sufficiency of Genentech's reason for its tardiness. The district court held that "MedImmune has pled no facts sufficient to assert that the PTO acted inappropriately in accepting the settlement documents from Genentech." No abuse of the district court's discretion has been shown, and no basis whatsoever for opening to collateral attack a discretionary decision of the PTO to accept a document in accordance with the rules of the PTO.

V

MedImmune states that if this court affirms the district court on the patent counts, the antitrust and unfair competition counts should be transferred to the Ninth Circuit. That procedure would violate the jurisdictional assignment to the Federal Circuit. In *Texas American Oil Co. v. Department of Energy*, 44 F.3d 1557, 1564 (Fed. Cir. 1995) (en banc) the court explained the assignment to the Federal Circuit of "case" jurisdiction, in recognition of the burdens of "issue" jurisdiction on litigants and on the courts.

As discussed in *Christianson v. Colt Indus. Operating Corp.*, 486 U.S. 800 (1988), the jurisdiction of the Federal Circuit is established by the well-pleaded complaint in the district court, whereupon the Federal Circuit must exercise jurisdiction of all of the issues in the case. In *United States v. Hohri*, 482 U.S. 64 (1987) the Court explained that the Federal Circuit must take jurisdiction of the appeal of all issues when the complaint includes any issue exclusively assigned to the Federal Circuit, in *Hohri* a nontax claim under the Little Tucker Act. *See also Atari, Inc. v. JS & A Group, Inc.*, 747 F.2d 1422, 1431 (Fed. Cir. 1984) (*en banc*) (Federal Circuit must exercise jurisdiction although only copyright issue was appealed). In *Holmes Group, Inc. v. Vornado Air Circulation Systems, Inc.*, 535 U.S. 826, 829 (2002) the Court confirmed that the jurisdiction of the Federal Circuit arises from the

complaint, and that the entire appeal is directed to the regional circuit when the patent count arose only by counterclaim. Similarly, when patent claims are included in order to manipulate the direction of the appeal, or are eliminated at the threshold of the pleading stage, the entire appeal is properly taken to the regional circuit. *E.g., Chamberlain Group, Inc. v. Skylink Techs. Inc.*, 381 F.3d 1178, 1189-90 (Fed. Cir. 2004); *Schwartzopf Dev. Corp. v. Ti-Coating, Inc.*, 800 F.2d 240, 245 (Fed. Cir. 1986) (referring to "the transient appearance of the [patent] counterclaim"). In all cases, the purpose is to avoid the burdens of dividing the appeal between two circuits. *See Texas American Oil*, 44 F.3d at 1564. It would be contrary to this careful balance and efficient design for the Federal Circuit to decide part of an appeal and then, depending on the outcome of that part, to ship the residue to another circuit.[4] The request to transfer part of this appeal to the Ninth Circuit is denied.

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[4] We take note of the dissent's argument that the case should now be sent to the Ninth Circuit for decision of the *Walker Process* and other patent/antitrust issues raised by the appellant, on the theory that the complaint should, after this appellate decision, be deemed to have been "constructively amended" to have been filed without the patent counts of the complaint. Neither statute nor precedent provides support for such a procedure, and indeed they weigh heavily against it. In none of the "authority" mentioned by the dissent was the complaint subject to retrospective amendment of well-pleaded issues after the legal status of the parties had been altered. The Court in *Christianson v. Colt* confirmed that jurisdiction "is determined by reference to the well-pleaded complaint, not the well tried case." 486 U.S. at 814; *see also Holmes Group v. Vornado Air Circulation Sys., Inc.*, 535 U.S. 826, 832, n.3 (2002). The purpose of the rule is to determine jurisdiction at the outset of litigation, to avoid throwing the parties into "a perpetual game of jurisdictional ping-pong." *Id.* at 818. To bifurcate an appeal after some of the issues are decided offers the worst of all possibilities, for it would not be known whether some issues would be shipped elsewhere, to be redocketed and rebriefed and reargued and reappealed, until after the Federal Circuit decided other issues. Such a situation is devoid of support.

We have considered all of the arguments raised by MedImmune. The decision of the district court is

AFFIRMED.

CLEVENGER, *Circuit Judge*, dissenting in part.

MedImmune, Inc. ("MedImmune") paid, and continues to pay, royalties under a 1997 licensing agreement with Genentech, Inc. ("Genentech"), which entitles MedImmune to produce and sell its humanized monoclonal antibody, Synagis®, free from liability under U.S. Patent No. 6,331,415 ("Cabilly II" or "the '415 patent"). Because MedImmune's good standing under the agreement necessarily quells any reasonable apprehension of an infringement suit brought by Genentech pursuant to the '415 patent, I agree with the court that the declaratory judgment claims properly were dismissed for want of jurisdiction. Indeed, the district court's dismissal is required by our prior decisions in *Gen-Probe, Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir. 2004) and *MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005). I write separately, however, to voice my disagreement with the court's refusal to transfer the remainder of the case to the Court of Appeals for the Ninth Circuit, pursuant to 28 U.S.C. § 1631, for a determination as to whether the district court properly granted summary judgment regarding MedImmune's antitrust and unfair competition claims.

Under 28 U.S.C. § 1295(a)(1), this court has exclusive jurisdiction over an appeal from a final decision of a district court, so long as the district court's jurisdiction was based in whole or in part upon 28 U.S.C. § 1338. *See Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1342 (Fed. Cir. 2003) (stating that if the district court had jurisdiction over at least one claim in the case under section 1338, then this court has appellate jurisdiction over the entire case). Section 1338(a) in turn provides that a district court shall have original jurisdiction over any civil action arising under an Act of Congress relat-

ing to patents. The "well-pleaded complaint" rule defines what "arising under" means. *See Holmes Group v. Vornado Air Circulation Sys., Inc.*, 535 U.S. 826, 833-34 (2002). "Under the well-pleaded complaint rule, as appropriately adapted to § 1338(a), whether a claim 'arises under' patent law must be determined from what necessarily appears in the plaintiff's statement of his own claim in the bill or declaration, unaided by anything alleged in anticipation or avoidance of defenses which it is thought the defendant may interpose." *Christianson v. Colt Indus. Operating Corp.*, 486 U.S. 800, 809 (1988) (internal quotation marks omitted). The focus of our jurisdictional inquiry should thus be upon MedImmune's complaint and whether, as ultimately amended, it arises under an Act of Congress relating to patents. *See Chamberlain Group v. Skylink Tech., Inc.*, 381 F.3d 1178, 1189 (Fed. Cir. 2004). As ultimately amended, I would hold that it does not.

Our precedent mandates this conclusion. First, we have stated that a dismissal for lack of subject matter jurisdiction is usually one without prejudice because the dismissing court has no power to render a judgment on the merits of the dismissed claim. *Textile Prods., Inc. v. Mead Corp.*, 134 F.3d 1481, 1486 (Fed. Cir. 1998). Such is the case here, and nothing about the district court's dismissal bars MedImmune from refiling its complaint. *See Semtek Int'l Inc. v. Lockheed Martin Corp.*, 531 U.S. 497, 505-06 (2001) ("The primary meaning of 'dismissal without prejudice,' we think, is dismissal without barring the defendant from returning later, to the same court, with the same underlying claim."). Second, we have held, in a decision that binds this panel, that dismissals without prejudice are "de facto amendments," or "constructive amendments," to the complaint. *See Nilssen v. Motorola, Inc.*, 203 F.3d 782, 784-85 (Fed. Cir. 2000) (noting that regardless of whether the patent claims were dismissed without prejudice or extinguished by amendment, the effect is the same because in either case the parties are left in the same legal position with respect to the patent claims as if they had never

been filed); *Gronholz v. Sears, Roebuck & Co.*, 836 F.2d 515, 516, 518 (Fed. Cir. 1987) (holding that plaintiff's voluntary dismissal of the patent claim without prejudice constituted an amendment to the complaint and that the suit no longer arose under the patent laws for jurisdictional purposes). Third, for jurisdictional determinations, we do not differentiate be tween actual and constructive amendments—"both divest us of jurisdiction if they eliminate all issues of patent law." *Chamberlain Group*, 381 F.3d at 1189.

Therefore, because the district court's dismissal of MedImmune's declaratory judgment claims without prejudice is equivalent for jurisdictional purposes to an amendment removing the declaratory judgment claims from the complaint, and because no other claims in MedImmune's complaint "arise under" patent law, the district court's dismissal eliminates all issues of patent law from MedImmune's well-pleaded complaint and thus divests this court of jurisdiction over the case. Where a plaintiff lacks standing to pursue a patent law claim, as in this case, we have no jurisdiction over the remaining claims and must transfer the case to an appropriate court of appeals. *See Fieldturf v. Southwest Recreational Indus.*, 357 F.3d 1266, 1267 (Fed. Cir. 2004). Indeed, MedImmune itself understands that a transfer is required if we affirm the absence of jurisdiction over the declaratory judgment claims. (Appellant's Reply Br. at 12 n.8.)

Finding no jurisdiction, I would transfer the case to the Court of Appeals for the Ninth Circuit, pursuant to 28 U.S.C. § 1631, for a determination as to whether the district court properly granted summary judgment regarding MedImmune's antitrust and unfair competition claims. *See Christianson*, 486 U.S. at 818-19 (noting that the Federal Circuit erred in deciding to reach the merits of plaintiff's antitrust claims after concluding that it lacked jurisdiction).

As the majority correctly notes, our jurisdiction is determined by the complaint. Where a patent law issue permeates

the complaint, the "case" is ours, and all "issues," including non-patent law issues, remain with us for decision. But when the complaint contains nary a whiff of patent law, as is the situation with the amended complaint in this case, we are powerless to adjudicate the other issues in the case.

To be sure, transfer to another circuit court involves some inconvenience to the parties and a burden on the courts. But inconvenience and burden are insufficient reasons to violate a fundamental limitation on federal courts: the power of judicial review vests only where jurisdiction lies.

**APPENDIX B**

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Apr. 26, 2004]

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Case No. CV 03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC., *et al.*

*Defendants.*

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AMENDED MEMORANDUM OF DECISION AND ORDER RE: Motion to Dismiss for Lack of Subject Matter Jurisdiction

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The Defendants' Motion to Dismiss for Lack of Subject Matter Jurisdiction came on for hearing on April 19, 2004 and this Court took the matter under submission. Having considered the parties' written and oral argument this court hereby GRANTS the Defendant' motion.

## INTRODUCTION

### I. Summary of Dispute

Plaintiff MedImmune is a biotechnology company whose most successful product is Synagis, a drug used to prevent serious lower respiratory tract disease in children. Amended Complaint ¶¶ 4-5. The Defendants are a biotechnology company, Genentech, Inc. ("Genentech") and a nonprofit organization, City of Hope, who are co-assignees of the patent in

dispute.[1] U.S. Patent No. 6,331,415B1 (issued December 18, 2001) ("'415 patent").

The '415 patent describes a method of producing monoclonal antibodies using recombinant deoxiribonuclic acid ("DNA") technology. *Id.* Synagis is a monoclonal antibody; MedImmune licenses the '415 patent for the production of its Synagis product. Amended Complaint, ¶ 18. Although MedImmune continues to fulfill its obligations under the license agreement, MedImmune asserts that the '415 patent is invalid, unenforceable and not infringed, and that MedImmune therefore does not owe the royalties it is paying to Genentech. Amended Complaint, ¶ 20, ¶¶ 131-64.

II. Status of Case

MedImmune originally made antitrust and unfair competition claims in addition to seeking declaratory judgment of invalidity, unenforceability, non-infringement, and lack of royalty obligation under the license agreement. Amended Complaint, ¶¶ 131-201. The antitrust and unfair competition claims were dismissed on summary judgment holding that the *Noerr-Pennington* doctrine applied to these claims. Memorandum of Decision and Order (filed Dec. 23, 2004, amended January 14, 2004). Consequently, the only claims remaining in this case are claims for declaratory judgment.

The parties fully briefed the issue of claim construction and this Court was prepared to hold the *Markman* hearing scheduled for March 15, 2004. However, prior to the *Markman* hearing a March 5, 2004 Federal Circuit decision suggested that this Court does not have subject matter jurisdiction. *See Gen-Probe, Inc. v. Vysis, Inc.*, 2004 WL 405737, *3 (Fed. Cir. 2004). On March 12, 2004, this Court stayed all other matters, including claim construction, until

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[1] References to Genentech in the remainder of this memorandum are intended to indicate both Genentech and City of Hope.

the issue of subject matter jurisdiction could be resolved. Telephonic Status Conference (held March 12, 2004).

III. Motion to Dismiss

In the Motion at issue here, Genentech seeks dismissal of all remaining causes of action based on lack of subject matter jurisdictions. Specifically, Genentech requests that the First Cause of Action (Declaratory Judgment on Contractual Rights and Obligations), the Second Cause of Action (Patent Invalidity), the Third Cause of Action (Patent Unenforceability), and the Fourth Cause of Action (Non-Infringement) be dismissed. Genentech's Notice of Motion and Motion to Dismiss for Lack of Subject Matter Jurisdiction (filed March 22, 2004) ("Motion").

The parties have briefed this issue for the Court. City of Hope joined Genentech's Motion to Dismiss but did not file a separate motion. City of Hope's Notice of Motion and Motion for Joinder in the Motion to Dismiss for Lack of Subject Matter Jurisdiction (filed March 23, 2004). MedImmune filed an Opposition and supported it with two Declarations. Plaintiff MedImmune, Inc's Opposition to Genentech, Inc.'s Motion to Dismiss (filed under seal, March 29, 2004) ("Opposition"); Declaration of David M. Scott in Support of Opposition to Motion to Dismiss for Lack of Subject Matter Jurisdiction (filed under seal, March 29, 2004); Declaration of Tanya Hunter in Support of Opposition to Motion to Dismiss for Lack of Subject Matter Jurisdiction (filed under seal, March 29, 2004). Genentech and City of Hope filed separate Reply memoranda. Genentech's Reply Brief in Support of Motion to Dismiss for Lack of Subject Matter Jurisdiction (filed April 5, 2004); Genentech's Request for Judicial Notice in Support of Motion to Dismiss for Lack of Subject Matter Jurisdiction (filed April 5, 2004) ("Notice Request"); Defendant City of Hope's Reply Brief in Support of Motion to Dismiss for Lack of Subject Matter Jurisdiction (filed April 5, 2004). This Court heard argument on April 19, 2004.

## LEGAL STANDARD

Genentech brings this Motion under Rules 12(b)(1) and 12(h)(3) of the Federal Rules of Civil Procedure ("FRCP"). Rule 12(b)(1) gives a party the option of presenting the defense of lack of subject matter jurisdiction by motion rather than asserting it in the responsive pleading. Rule 12(h)(3) makes it clear that subject matter jurisdiction is a defense that is never waived: "Whenever it appears by suggestion of the parties or otherwise that the Court lacks jurisdiction of the subject matter, the court *shall* dismiss the action." FRCP Rule 12(h)(3) (emphasis added). If a court lacks subject matter jurisdiction, dismissal of the action is mandatory. *See Ex parte McCardle*, 74 U.S. 506, 514 (1868).

## DISCUSSION

### I. The Gen-Probe Decision

Article III of the Constitution authorizes the federal judiciary to hear justiciable cases and controversies. To effectuate this requirement, the Declaratory Judgment Act requires that there be an "actual controversy" between the parties. 28 U.S.C. § 2201(a); see also *Gen-Probe*, 2004 WL 405737, *3. It is therefore the rule that a declaratory judgment plaintiff must establish that the "totality of the circumstances" demonstrates that an actual controversy exists. *Gen-Probe*, 2004 WL 405737 at *3.

In the past, the "actual controversy" requirement has not been interpreted as precluding a licensee from challenging a patent it licenses. *See C.R. Bard Inc. v. Schwartz*, 716 F.2d 874, 875 (Fed Cir. 1983) ("[A] patent license need not be terminated before a patent licensee may bring a declaratory judgment action"); *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969) (holding that a license does not bar the licensee from challenging the validity of the patent).

In *Gen-Probe*, however, the Federal Circuit limited the ability of licensees to challenge the patents they license. The Court held that no actual controversy existed between a patentee and a licensee in good standing. *Gen-Probe*, 2004 WL 405737 at *4 (noting that the "license, unless materially breached, obliterated any reasonable apprehension of a lawsuit based on the prior circumstances cited by the district court for jurisdiction.").

*Gen-Probe* distinguished prior cases as involving plaintiff-licensees who were not in good standing. The plaintiff-licensee in Gen-Probe, like MedImmune in this case, sought declaratory judgment of patent invalidity, unenforceability or non-infringement. *See Gen-Probe*, 2004 WL 405737. As is true of the plaintiff in this case, the plaintiff in *Gen-Probe* made these challenges while continuing to: fulfill its obligations under the license agreement. *Gen-Probe*, 2004 WL 405737 at *4. The Federal Circuit found the Gen-Probe plaintiff's continued performance of the license agreement to be a critical factor that destroyed jurisdiction by eliminating any reasonable apprehension of suit by the licensor for infringement.

II. Controlling Law

MedImmune essentially admits that under *Gen-Probe* this Court does not have jurisdiction, but argues that *Gen-Probe* is not controlling. MedImmune contends that this Court has jurisdiction because Ninth Circuit precedent does not require that a license be breached before the licensee can seek declaratory relief. Opposition at 10 (citing *Hal Roach Studios, Inc. v. Feiner & Co.*, 896 F.2d 1542 (9th Cir. 1987)).

For issues not unique to patent law, this Court must apply the law of the Ninth Circuit. MedImmune seeks to characterize subject matter jurisdiction as a procedural matter that is unrelated to patent law and thus to have this Court apply Ninth Circuit law rather than that of the Federal Circuit.

Opposition at 5-7 (citing *Toxgon Corp. v. ENFL, Inc.*, 213 F.3d 1379, 1380 (Fed. Cir. 2002; *Molins PLC v. Quigg*, 837 F.2d 1064, 1066 (Fed. Cir. 1988); *Vanguard Research, Inc. v. Peat, Inc.*, 304 F.3d 1249, 1254 (Fed. Cir. 2002)).

Federal Circuit precedent controls the Court's decision in this case. Determination of whether an actual controversy exists under these facts requires evaluation of whether a licensee has a reasonable apprehension of a claim of infringement. This decision clearly implicates patent law, and is well within the purview of the Federal Circuit. See *Shell Oil Company v. Amoco Corp.*, 970 F.2d 885, 887-888 (Fed. Cir. 1992) ("The reasonable apprehension of a threat of patent infringement "clearly implicates" the patent law; the law of this circuit therefore applies.").

The cases that MedImmune cites do not support the application of anything other than the law of the Federal Circuit. *Toxgon, Molins*, and *Vanguard Research* do indicate that the law of the regional circuit should govern procedural issues, but they also support the proposition that when jurisdictional questions are intertwined with patent law considerations, the law of the Federal Circuit applies.

In *Toxgon* the Federal Circuit reviews a District Court's decision to dismiss the case for lack of subject matter jurisdiction. The court applies Ninth Circuit law to decide the correct standard under which it will review the dismissal; regional circuit law is applied to this procedural question. 312 F.3d at 1380-81. However, when deciding whether the District Court correctly interpreted the jurisdictional implications of a statute immunizing federal contractors from patent infringement suits, the *Toxgon* Court looked to Supreme Court and Federal Circuit precedent. 312 F.3d at 1381-82. When resolving a jurisdictional issue that involved patent concerns, the *Toxgon* court used the law of the Federal Circuit.

Like *Toxgon*, *Vanguard Research* states that the regional circuit is the appropriate source of law for "procedural issues not unique to patent law." 304 F.3d at 1254. However, in considering whether the plaintiff had a reasonable apprehension of suit that would create an actual controversy, the question at issue before this Court, the *Vanguard Research* court applied Federal Circuit law. 304 F.3d at 1254-55. When the *Vanguard Research* Court faced the situation that this Court now faces—determining whether a plaintiff has an actual controversy with a patentee—the *Vanguard Research* Court looked to the law of the Federal Circuit.

Similarly, in *Molins* the court held that the law of the regional circuit will apply to a question, like the ripeness question being considered in *Molins*, "which does not pertain to patent law issues and has no effect on this court's jurisdiction." 837 F.2d at 1066. Far from indicating that regional law applies in this case, the above-quoted statement in *Molins* suggests its converse: that application of regional law is inappropriate when considering questions that do pertain to patent law issues.[2] *Molins* thus further supports the conclusion that when a jurisdictional issue involves patent law concerns—such as the threat of infringement litigation between a patentee and a licensee—Federal Circuit law controls.

This Court's jurisdiction over this case depends on whether a patent licensee in good standing has an actual controversy with a patentholder whose patent the plaintiff-licensee believes is invalid, unenforceable, or not infringed. This jurisdictional issue is intertwined with patent law considerations, thus the law of the Federal Circuit controls. 28 U.S.C. § 1295 (giving the Federal Jurisdiction over appeals if

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[2] Ripeness was also the issue in *Shell Oil*; because the ripeness question in that case depended on interpretation of a statute relevant to patent law, the *Shell Oil* Court applied the law of the Federal Circuit. *Shell Oil*, 970 F.2d at 888, n.10.

the jurisdiction of the District Court was based on 28 U.S.C. § 1338, which grants exclusive jurisdiction to the federal courts in cases arising under the patent laws).

III. Subject Matter Jurisdiction

Federal Circuit precedent dictates that this case be dismissed. *Gen-Probe* held that a licensee in good standing cannot seek relief under the Declaratory Judgment Act. 2004 WL 405737 at *6. Because MedImmune is a licensee in good standing, and because the relief MedImmune seeks is for declaratory judgment, this Court has no choice but to dismiss this case for lack of subject matter jurisdiction.

A. MedImmune is a Licensee in Good Standing

MedImmune is a licensee of the '415 patent and is in good standing. MedImmune's First Amended Complaint says:

> With its New Cabilly Patent in hand, Genentech immediately exercised its illegally obtained monopoly by advising MedImmune that the New Cabilly Patent covers MedImmune's Synagis® product. As a consequence of this assertion, MedImmune began to make and continues to make significant payments to Genentech under an agreement entered into by MedImmune and Genentech on or about June 5, 1997 (the "1997 License Agreement"). This 1997 License Agreement provided rights to various intellectual property, including the patent application that later matured into the New Cabilly patent. After issuance of the New Cabilly Patent, MedImmune was forced to obtain additional license agreements from Genentech on or about February 7, 2003—at substantial cost—to cover seven new products that MedImmune has been developing (the "2003

> License Agreements") (collectively the 1997 and 2003 License Agreements are referred to herein as the "License Agreements").

FAC ¶ 18. There is no dispute that MedImmune is a licensee in good standing of the patent it seeks to challenge.

B. MedImmune Seeks Declaratory Judgment

Each of the claims remaining in this case are for declaratory judgment. The First Amended Complaint ("FAC") states:

> MedImmune also seeks a declaration that: (a) the New Cabilly Patent (which is co-owned by Genentech and COH) is invalid; (b) the New Cabilly Patent is unenforceable; (c) MedImmune's sales of its Synagis® product do not infringe any valid claim of the New Cabilly Patent; and (d) MedImmune owes no payments to Genentech under the License Agreements.

FAC ¶ 20; see also ¶¶ 131-33 (seeking declaratory judgment on contractual rights and obligations); ¶¶ 134-39 (seeking declaratory judgment that the New Cabilly patent is invalid); ¶¶ 140-61 (seeking declaratory judgment that the New Cabilly patent is unenforceable); ¶¶ 162-64 (seeking declaratory judgment that the Synagis® product does not infringe any valid and enforceable claim of the New Cabilly patent). As is indicated by the foregoing, the claims that remain at issue in this case are all claims for declaratory judgment.

C. Mandatory Dismissal

In *Gen-Probe* the Federal Circuit determined that controversies over patent validity, enforcement, infringement would not be recognized while license agreements protected the licensee from suit for infringement. The *Gen-Probe* panel was concerned by the "undesirable result" that licensors would bear more risk and be less likely to grant licenses if

licensees were permitted to challenge the patents they license. 2004 WL 405737, *6. The panel was apparently more persuaded by this concern than by the potential that invalid or unenforceable patents will stand because licensees will be too risk-averse to challenge them.

Requiring licensees to violate their license agreements and subject themselves to infringement suits before recognizing that they have an actual controversy with their licensors forces licensees to take a tremendous risk to challenge a patent, one that some with valid claims will likely be unwilling to take. The Federal Circuit has commented on the chilling effect this will have on patent challenges:

> To always require the termination of a license agreement as a precondition to suit would mean that a licensee must then bear the risk of liability of infringement. This would discourage licensees from contesting patent validity and would be contrary to the policies expressed in Lear.

*C.R. Bard, Inc. v. Schwartz*, 716 F.2d 874, 880 (Fed. Cir. 1983).

The public has a strong interest in ferreting out invalid or unenforceable patents and in ensuring that the owners of valid patents monopolize only the technology claimed by the patent. The Supreme Court has described the importance of allowing licensees to challenge the patents they license:

> Surely the equities of the licensor do not weigh very heavily when they are balanced against the important public interest in permitting full and free competition in the use of ideas which are in reality a part of the public domain. Licensees may often be the only individuals with enough economic incentive to challenge the patentability of an inventor's discovery. If they are muzzled, the public may continually be required to pay tribute to would-be monopolists without need or justification.

*Lear v. Adkins*, 395 U.S. 653 (1969). Licensees may cham-

pion the public interest in eliminating the monopoly over subject matter that is not rightfully acquired; stifling their challenges risks losing to private parties property that actually belongs to the public.

Even if it has serious misgivings about the panel's conclusion, this Court is not free to reconsider policy ramifications that *Gen-Probe* rejected. There are no relevant facts that distinguish this case from the facts of *Gen-Probe*. *Gen-Probe* is controlling law, and it dictates that this case be dismissed for lack of an actual controversy. Because *Gen-Probe* ruled that no subject matter jurisdiction exists under these facts, this Court must grant Genentech's Motion. FRCP Rule 12(h)(3).

## CONCLUSION

Because the *Gen-Probe* decision dictates that this Court does not have subject matter jurisdiction over MedImmune's suit for declaratory judgment, Genentech's Motion is GRANTED and the First, Second, Third, and Fourth Causes of Actions are dismissed as to both Genentech and City of Hope.

IT IS SO ORDERED.

DATED: April 23, 2004

/s/ Mariana R. Pfaelzer
HONORABLE MARIANA R. PFAELZER
United States District Judge

## APPENDIX C

CONSTITUTIONAL AND STATUTORY PROVISIONS

Article III of the Constitution of the United States provides in relevant part:

> SECTION 2. The judicial Power shall extend to all Cases, in Law and Equity, arising under this Constitution, the Laws of the United States . . . .

Title 28 U.S.C. § 1331 provides:

> The district courts shall have original jurisdiction of all civil actions arising under the Constitution, laws, or treaties of the United States.

Title 28 U.S.C. § 1338(a) provides:

> The district courts shall have original jurisdiction of any civil action arising under any act of Congress relating to patents, plant variety protection, copyrights and trademarks. Such jurisdiction shall be exclusive of the courts of the states in patent, plant variety protection and copyright cases.

Title 28 U.S.C. § 2201(a) provides:

> In any case of actual controversy within its jurisdiction, except . . . any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested party seeking such a declaration, whether or not further relief is or could be sought. Any such declaration shall have the force and effect of a final judgment or decree and shall be reviewable as such.

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No. 05-608

Supreme Court, U.S.
FILED
DEC 27 2005
OFFICE OF THE CLERK

# In the Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner*,

v.

GENENTECH, INC., et al.,

*Respondents*.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

## BRIEF IN OPPOSITION

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## QUESTION PRESENTED

Whether the Declaratory Judgment Act gives a patent licensee special rights to commence a declaratory judgment action for patent non-infringement and invalidity against its licensor, when such licensee enjoys all benefits and protections of the license, faces no threat of an infringement suit, and indeed is immune from any suit on the patent.

## RULE 29.6 STATEMENT

Approximately 56% of the issued common stock of Respondent Genentech, Inc. is owned by Roche Holdings, Inc. Respondent Genentech, Inc. remains an independent, publicly traded company.

Respondent City of Hope is a non-profit biomedical research, treatment and educational institution. City of Hope has no parent company. No entity owns stock in City of Hope.

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## STATEMENT OF THE CASE

This case concerns the actions of a party that, for the express purpose of avoiding any risk of an infringement suit, requested and secured licenses to patented technology, and then, after securing the last of the licenses, sued the patent-holder under the Declaratory Judgment Act, claiming there was a live controversy over the validity, enforceability and infringement of the patent.

### A. The License

Respondents Genentech, Inc. ("Genentech") and City of Hope collaborated over several years to develop recombinant DNA technology to produce antibody molecules to help treat cancer and other diseases. The results of this collaboration included the patent-in-suit U.S. Patent No. 6,331,415 ("the '415 patent"). Genentech uses this technology in five of its marketed products, including treatments for certain types of breast and colorectal cancer. It also licenses this technology to other companies who wish to use it.

Petitioner MedImmune, Inc. ("MedImmune") is a biotechnology company whose products include genetically engineered antibodies. Pet. App. 21a-22a. One of its currently marketed products, Synagis®, and many of its pipeline products, are made using patented technology owned by Genentech and City of Hope. Pet. App. 21a-22a.

There was a lengthy dispute between Genentech and a British company, Celltech R&D, Ltd., over the U.S. patent rights in the relevant invention. Pet. App. 2a-4a.[1] While that dispute was pending, MedImmune obtained licenses from both Genentech and Celltech. Pet. App. 4a. In June 1997,

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[1] MedImmune misstates the facts relating to the priority contest in the United States Patent and Trademark Office ("PTO") and the resolution of the district court litigation that followed. Pet. at 2-3 & n.2. The Federal Circuit correctly summarized the undisputed material facts relating to these events. Pet. App. 2a-4a.

MedImmune entered into a license agreement with Genentech that permitted MedImmune to practice U.S. Patent No. 4,816,567 ("the '567 patent," claiming related technology), and any patent that issued from a pending Genentech application. Pet. App. 4a. The Genentech application ultimately matured into the '415 patent which claims the invention at issue. Pet. App. 4a. MedImmune has no products covered by the '567 patent and has not paid royalties on the '567 patent.

The '415 patent issued in 2001, after the resolution of the priority dispute between Genentech and Celltech. Pet. App. 3a-4a. Genentech thereafter advised MedImmune of its belief that Synagis® was a "licensed product" for which royalties were due. Pet. App. 4a. MedImmune balked at first, denying that Synagis® was a "licensed product."[2] Pet. App. 4a. But MedImmune subsequently agreed to pay royalties (albeit "under protest"), because, as its General Counsel later testified, MedImmune wanted to retain the benefits of the license – and not be subject to an infringement suit – if its challenge to the patent failed. C.A.A. 314, 3291-92. MedImmune later requested and entered into seven separate agreements to license the '415 patent for products in development. Pet. App. 28a.

Shortly after securing the last of these license agreements, MedImmune filed this declaratory judgment action to invalidate the '415 patent and for a judgment that Synagis® did not infringe the '415 patent. Pet. App. 4a. At all times relevant to this case, however, MedImmune

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[2] The relevant Genentech-MedImmune license granted rights conditionally: if a particular MedImmune product was a "licensed product" (meaning it infringed at least one valid claim of a Genentech patent), MedImmune could secure a license for that product by paying specified royalties. C.A.A. 3584. (Citations to "C.A.A." are to the joint appendix filed in the Court of Appeals.) MedImmune thus could have disputed that Synagis® was a "licensed product" under the existing license agreement.

remained a licensee in good standing and made clear its intent not to breach the Synagis® license agreement. C.A.A. 314. It thus retained all benefits of the license, including protection from all of the remedies at law or in equity for patent infringement, such as an injunction, treble damages, and a court-determined, non-contractual royalty rate. Under such circumstances, Genentech could not sue MedImmune for patent infringement, and could not cancel the license agreement.

### B. The District Court and Federal Circuit Decisions

While this case was pending in the District Court, the Federal Circuit issued its decision in *Gen-Probe, Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir.), *cert. dismissed*, 125 S. Ct. 351 (2004), holding that as a general rule a patent licensee in good standing does not have the "reasonable apprehension of a lawsuit" that, under longstanding law, is necessary to maintain a declaratory judgment action. MedImmune acknowledged that it had no reasonable apprehension of suit. Pet. App. 4a. The District Court, by order entered April 27, 2004, dismissed MedImmune's declaratory judgment action for lack of subject matter jurisdiction. Pet. App. 21a-31a.

In the Court of Appeals, MedImmune nominally tried to distinguish *Gen-Probe*. Pet. App. 5a. But MedImmune primarily argued that, although it is "free of apprehension of suit" (Pet. App. 4a), patent licensees have the absolute right under this Court's decision in *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969), to bring declaratory judgment actions to challenge the validity of licensed patents (Pet. App. 4a-5a). The Federal Circuit disagreed, concluding that the facts of this case do not present "a 'definite and concrete controversy' of 'sufficient immediacy and reality' to warrant judicial intervention." Pet. App. 8a (quoting *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240 (1937), and *Md. Cas. Co.*

*v. Pac. Coal & Oil Co.*, 312 U.S. 270, 273 (1941)) (internal citations omitted).

The Federal Circuit explained that in *Lear* this Court eliminated the doctrine of "licensee estoppel," a substantive rule of patent law, and did not consider declaratory judgment standards at all: "In *Lear* the licensee stopped paying royalties and the patentee sued for royalties; there was clearly a justiciable controversy, and that aspect was not an issue in *Lear*." Pet. App. 5a. In contrast, "the issue here is not one of estoppel, but of availability of the declaratory judgment procedure." Pet. App. 6a. The court explained that because in this case "there is no defaulting licensee and no possibility of suit," the fundamental requirements of Article III are not satisfied. Pet. App. 6a. The Federal Circuit grounded its analysis in this Court's precedents concerning when a controversy is sufficiently ripe and concrete to support a declaratory judgment action. Pet. App. 8a (citing *Aetna*, 300 U.S. at 241; *Md. Cas. Co.*, 312 U.S. at 273; *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 96 (1993)).

The Federal Circuit next addressed MedImmune's argument, recycled here, that "cases from other circuits hold that a licensee need not terminate its license in order to acquire declaratory standing." Pet. App. 7a. The court explained that "in each of the cited cases there was an additional factor, such as money owed on the contract, or the plaintiff or its indemnitee had been threatened with suit, or there was a change in circumstances which affected performance of the contract, meeting the constitutional and statutory requirements that there must be an actual controversy in order to invoke judicial authority." Pet. App. 7a. Thus, there was no conflict with other circuits.

Last, the Federal Circuit rejected MedImmune's policy arguments, in particular the notion that the public interest in challenging potentially invalid patents required giving licensees a one-sided option to litigate licensed patents. The

court stressed two points. First, patent-specific issues could "not create a policy-driven exception" to the constitutional and statutory requirements of an actual controversy. Pet. App. 7a. Second, it would be inequitable for the patent owner, "having contracted away its right to sue," to be under a "continuing risk of attack on the patent whenever the licensee chooses – for example if the product achieves commercial success – while the licensee can preserve its license and royalty rate if the attack fails." Pet. App. 7a. A one-sided option to sue at will, the court reasoned, "distorts the equalizing principles that underlie the Declaratory Judgment Act." Pet. App. 7a.

### C. The Pending Reexamination of the '415 Patent

After the District Court dismissed MedImmune's federal lawsuit challenging the '415 patent, a law firm on behalf of an unidentified client filed with the PTO a request for *ex parte* reexamination of the validity of the '415 patent. The PTO granted the request in July 2005, and on September 13, 2005, the PTO issued an Office Action rejecting the claims of the '415 patent for "obviousness-type double patenting." Genentech filed its response to the Office Action on November 25, 2005, and is awaiting further action by the PTO.

## REASONS FOR DENYING THE WRIT

The petition should be denied for three reasons. First, the Federal Circuit's decision is consistent with the declaratory judgment jurisprudence of this Court and the courts of appeals. The Declaratory Judgment Act permits persons who anticipate an inevitable lawsuit to come to court first, before damages accrue, for a declaration that they are not liable to the feared opponent. It is nevertheless black letter law that a declaratory judgment action, no less than any other suit, must present a live case or controversy and not seek a merely advisory decree. In enforcing this

requirement, the Federal Circuit and the other courts of appeals ask, among other things, whether a declaratory judgment plaintiff has a "reasonable apprehension" that it will be sued by the declaratory judgment defendant. If not, there is no actionable controversy. Because MedImmune admitted it had no apprehension of suit, and could cite no other case-specific circumstances establishing a live controversy between the parties, the Federal Circuit ruled there was no case or controversy here.

That analysis is an unremarkable application of settled law. MedImmune claims, however, that because it is a *patent licensee*, it has special rights under decisions of this Court to challenge licensed patents at any time of its choosing – even if, under ordinary standards, there is no Article III controversy. It claims patent licensees *may* seek advisory decrees regarding what *would* happen *if* they abandoned the protections of their licenses *and* were sued for infringement. There is no support for that proposition in this Court's Article III cases, nor in *Lear*. Nor is this question close enough to merit review.

No declaratory judgment case of this Court has featured a plaintiff immune from suit, as MedImmune is here by virtue of its license to the '415 patent. Hence, none of the Federal Circuit's rulings could be in any direct conflict with this Court's cases. Since *Ashwander v. Tennessee Valley Authority*, 297 U.S. 288 (1936), moreover, this Court consistently has held that federal courts do not have jurisdiction to issue merely advisory opinions under the Declaratory Judgment Act. All of this Court's cases have involved a "definite and concrete controversy" (*Aetna*, 300 U.S. at 240) of "sufficient immediacy and reality" (*Md. Cas. Co.*, 312 U.S. at 273) to warrant judicial intervention.

As for the circuit cases cited in the petition, they typically involved some "additional factor" beyond the mere existence of a license or contract between the parties that demonstrated the existence of a live controversy. Pet. App.

7a. Variations in the outcomes of these cases reflect the fact-bound application of settled law to different circumstances, not any disagreement over the governing legal principles.

Second, the Federal Circuit's decision does not conflict with *Lear*. *Lear* was not a declaratory judgment action; it was a royalty collection action that presented a justiciable controversy. Accordingly, *Lear* neither holds nor says anything about when a declaratory judgment action is appropriate. *Lear* instead eliminated the substantive patent law "licensee estoppel" doctrine that prevented licensees from ever disputing the validity of a patent – even if the licensee had ceased paying royalties and had already been sued by the licensor. Nothing about *Lear* requires the extraordinary further leap urged by MedImmune: that licensees must *always* be free to challenge the validity of patents irrespective of the "actual controversy" requirement of the Declaratory Judgment Act and Article III.

Third, MedImmune's policy arguments do not, and could not, justify making an exception to bedrock Article III principles for patent licensees. The "case or controversy" requirement is a limitation on the constitutional jurisdiction of the federal courts, which cannot be exceeded no matter the asserted justification. Regardless, neither the integrity of the patent system nor the progress of medical science depends on allowing licensees in good standing to challenge the validity of licensed patents. So-called "weak" patents can be challenged in a variety of ways and settings, including through the administrative "reexamination" process by which the PTO is presently reviewing the very patent at issue in this case. The "need" to create a heretofore unknown exception to the case or controversy requirement is not nearly as great as MedImmune claims.

MedImmune identifies no genuine conflict and offers no persuasive justification for the expansion of settled precedent that it seeks. The petition should be denied.

## I. THE FEDERAL CIRCUIT'S DECISION APPLIES WELL ESTABLISHED PRINCIPLES TO FACTS THAT PRESENT NO CASE OR CONTROVERSY.

A claim under the Declaratory Judgment Act, 28 U.S.C. § 2201(a), must present "a concrete case admitting of an immediate and definitive determination of the legal rights of the parties in an adversary proceeding." *Aetna*, 300 U.S. at 241. To determine whether a declaratory judgment case is sufficiently concrete, courts adjudicating patent cases have long applied the "reasonable apprehension of suit" test, which inquires whether a declaratory judgment plaintiff faces a threat of suit from the patent owner. *See Japan Gas Lighter Ass'n v. Ronson Corp.*, 257 F. Supp. 219, 237 (D.N.J. 1966) (first formulating test). The Federal Circuit has applied that test for decades in cases where the plaintiff seeks a declaration that a competitor's patent is invalid, or not infringed.[3] The "reasonable apprehension" test also has been employed by every circuit and in many analogous circumstances, including copyright, trademark, trade secrets, "right of publicity," unfair trade practices, unfair labor practices, and breach of contract cases.[4]

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[3] *See Jervis B. Webb Co. v. Southern Sys., Inc.*, 742 F.2d 1388, 1398-99 (Fed. Cir. 1984) (explaining that the defendant "must have engaged in conduct that created on the part of the declaratory plaintiff a reasonable apprehension that it will face an infringement suit if it commences or continues the activity in question"); *see also Teva Pharm. USA, Inc. v. Pfizer, Inc.*, 395 F.3d 1324, 1334 (Fed. Cir.) (holding that the declaratory judgment plaintiff was "unable to demonstrate a reasonable apprehension of imminent suit on the part of [the declaratory judgment defendant] for [patent] infringement"), *cert. denied*, 126 S. Ct. 473 (2005).

[4] *See, e.g., Sallen v. Corinthians Licenciamentos LTDA*, 273 F.3d 14, 25 (1st Cir. 2001) ("The reasonable apprehension of suit doctrine exists to cabin declaratory judgment actions where the only controversy surrounds a potential, future lawsuit."); *Starter Corp. v. Converse, Inc.*, 84 F.3d 592 (2d Cir. 1996) (applying Federal Circuit's "reasonable apprehension" test to trademark case); *Interdynamics, Inc. v. Wolf*, 698

A straightforward application of the reasonable apprehension rule to the facts of this case leads to the conclusion that no case or controversy exists. MedImmune

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F.2d 157, 166 (3d Cir. 1982) (applying the legal principles set forth by the Seventh Circuit in *International Harvester Co. v. Deere & Co.*, 623 F.2d 1207, 1210-11 (7th Cir. 1980), and noting that the standard "provides what is perhaps the most comprehensive formulation of the test that a court should apply in determining whether [the court has jurisdiction] to grant declaratory relief in a patent case"); *Volvo Constr. Equip. N. Am., Inc. v. CLM Equip. Co.*, 386 F.3d 581, 593-94 (4th Cir. 2004) (holding that declaratory judgment jurisdiction existed because plaintiff "possessed a reasonable apprehension of a multiplicity of litigation and of liability for ongoing damages"); *Texas v. West Publ'g Co.*, 882 F.2d 171, 175 (5th Cir. 1989) (applying Federal Circuit's "basic declaratory judgment principles [that] are well settled" to copyright case); *Robin Prods. Co. v. Tomocek*, 465 F.2d 1193, 1196 (6th Cir. 1972) (phrasing the test as whether a "reasonable man" would regard the threatened action as a "charge of infringement"); *Int'l Harvester Co. v. Deere & Co.*, 623 F.2d 1207, 1210-11 (7th Cir. 1980) (referenced above); *Crown Drug Co. v. Revlon, Inc.*, 703 F.2d 240, 243 (7th Cir. 1983) (applying reasonable apprehension test to dismiss plaintiff's action for a declaration that it was not liable for unfair trade practices); *Sherwood Med. Indus., Inc. v. Deknatel, Inc.*, 512 F.2d 724, 728-29 (8th Cir. 1975) (holding that a combination of factors gave rise to a reasonable apprehension of infringement litigation); *Nat'l Basketball Ass'n v. SDC Basketball Club, Inc.*, 815 F.2d 562, 566 (9th Cir. 1987) (applying the reasonable apprehension test to a contract dispute between NBA and a franchisee); *Cardtoons, L.C. v. Major League Baseball Players Ass'n*, 95 F.3d 959, 965-66 (10th Cir. 1996) (applying reasonable apprehension of litigation test to "right of publicity" case and citing with approval several Federal Circuit declaratory judgment jurisdiction cases); *GTE Directories Publ'g Corp. v. Trimen Am.*, 67 F.3d 1563, 1569 (11th Cir. 1995) (applying reasonable apprehension of suit test); *United Christian Scientists v. Christian Sci. Bd. of Dir.*, 829 F.2d 1152, 1159 (D.C. Cir. 1987) (applying reasonable apprehension of litigation test to copyright dispute and citing with approval the application of the test in the Federal Circuit and other circuits); *Fed. Express Corp. v. Air Line Pilots Ass'n*, 67 F.3d 961, 964-65 (D.C. Cir. 1995) (applying the test to determine whether the court could rule on an assertion of unfair labor practices).

admitted that it runs *no* risk of suit and that it intends to remain a licensee in good standing precisely to avoid the risk of suit. Pet. App. 4a. Thus, MedImmune has no apprehension of suit whatsoever, reasonable or otherwise. Nor can MedImmune point to any unique facts here that establish a justiciable controversy notwithstanding the immunity from suit it enjoys as a licensee. Notably, MedImmune does not in its petition ask this Court to review or reject the "reasonable apprehension of suit" test. It seeks instead a patent licensee exception to that test – and to Article III itself.

MedImmune argues that there is a justiciable controversy because it *would* have a reasonable apprehension of suit *if* it stopped paying license royalties. Pet. App. 5a. MedImmune thus seeks to base Article III jurisdiction on an entirely hypothetical controversy, while it continues to pay royalties precisely to ensure that no *actual* controversy can arise. That is not sufficient. This Court long ago declared that federal courts have no jurisdiction to issue "an opinion advising what the law would be upon a hypothetical set of facts." *Aetna*, 300 U.S. at 241.

Courts of appeals hold the same. In *Hendrix v. Poonai*, 662 F.2d 719 (11th Cir. 1981), for example, the Eleventh Circuit, in denying declaratory judgment jurisdiction, explained that Article III courts are not empowered to advise litigants regarding such strategic business decisions:

> Persons occupying positions of responsibility, like the appellants, often must make difficult decisions that can have adverse consequences for others. The possibility of being sued by those adversely affected is an inherent risk faced by the decisionmakers. Needless to say, the decisionmakers would benefit greatly by having guidance as to the potential legal ramifications of their decisions. Furnishing

> such guidance prior to the making of the decision, however, is the role of counsel, not of the courts.

*Id.* at 722.

In *Crowley Cutlery Co. v. United States*, 849 F.2d 273 (7th Cir. 1988), Judge Posner made the same point, explaining that

> intentions alone do not make a case or controversy in the constitutional sense. You cannot go to a federal court for advice on the legality of a proposed course of action. You must be a party to an existing legal dispute. This is true whether you are seeking a declaratory judgment or any other form of relief; the declaratory-judgment statute cannot amend Article III.

*Id.* at 276.[5] MedImmune's claim does not meet the basic legal requirements for establishing a case or controversy.

Furthermore, MedImmune argues for a rule that would be unprecedented in the annals of declaratory relief law: that patent licensees should have the *unilateral* right to declare a justiciable controversy and sue the patent owner even though the license bars any infringement suit by the patent owner against the licensee. It is well established that a patent-

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[5] *See also, e.g., Harris Trust & Sav. Bank v. E-II Holdings, Inc.*, 926 F.2d 636, 640 n.14 (7th Cir. 1991) (explaining that the Declaratory Judgment Act "was never intended as a device for relegating to the courts responsibilities reposed initially in private parties" (internal quotation marks and citation omitted)); *Brown & Root, Inc. v. Big Rock Corp.*, 383 F.2d 662, 666 (5th Cir. 1967) ("However desirable such a decision may be to the parties, and however much the Court may sympathize with their desires, it is fundamental that the question of Federal jurisdiction is always present and if there be no jurisdiction the courts must decline to act.").

holder who has licensed its patents has given up its right to file suit against the licensee for infringement of those patents. *See Spindelfabrik Suessen-Schurr, Stahlecker & Grill GmbH v. Schubert & Salzer Maschinenfabrik Aktiengesellschaft*, 829 F.2d 1075, 1081 (Fed. Cir. 1987) (A "patent license agreement is in essence nothing more than a promise by the licensor not to sue the licensee."). Thus MedImmune proposes a one-sided rule that would destroy the *mutuality* of access to the courts that is the very reason for the existence of the Declaratory Judgment Act.

As the Federal Circuit has observed,

> The purpose of the [Declaratory Judgment] Act is to enable a person who is reasonably at legal risk because of an unresolved dispute, to obtain judicial resolution of that dispute without having to await the commencement of legal action by the other side. It accommodates the practical situation wherein the interests of one side to the dispute may be served by delay in taking legal action.

*BP Chem. Ltd. v. Union Carbide Corp.*, 4 F.3d 975, 977 (Fed. Cir. 1993); *see also EMC Corp. v. Norand Corp.*, 89 F.3d 807, 814-15 (Fed. Cir. 1996). The Declaratory Judgment Act equalizes the parties' positions by giving both sides access to the courts under the same standards. If one party has a cause of action, the other party can sue as well and "clear the air." *EMC Corp.*, 89 F.3d at 815 (internal quotation marks and citation omitted). The contrary regime MedImmune urges, with unilateral rights of suit for patent licensees only, has no support in the law.

## II. THE FEDERAL CIRCUIT'S DECISION DOES NOT CONFLICT WITH THE CASES CITED BY MEDIMMUNE.

### A. The Federal Circuit's Decision Does Not Conflict With This Court's Declaratory Judgment Jurisprudence.

The Federal Circuit's determination that there is no justiciable controversy under the facts of this case is consistent with this Court's declaratory judgment jurisprudence. In each case in which this Court has found a declaratory relief action proper, the declaratory judgment plaintiff faced a very real and often imminent threat of litigation, or other facts established the existence of a ripe controversy. None involved a declaratory judgment plaintiff, like the one in this case, who had no present controversy and who was *immune* from suit.

*Aetna*, for example, involved a declaratory judgment suit by an insurer against an insured *who had stopped paying premiums* on the ground that his disability relieved him of the obligation to make such payments. *Aetna*, 300 U.S. at 242. The Court held this cessation of premium payments created an immediate controversy. The insurer's position that the insured had wrongfully breached the policy required immediate resolution to determine whether the insurer needed to maintain financial reserves for the policy. *Id.* at 239, 242. This Court also emphasized that the insured had the right to sue at any time to demand payment of the policy's cash value. *Id.* at 243-44.

Nor is there any conflict with *Altvater v. Freeman*, 319 U.S. 359 (1943). In *Altvater*, there was a "raging" dispute between the parties, reflected in a history of multiple claims and counterclaims. *Id.* at 361-62, 364. This Court held that where the counterclaimant was paying royalties "under compulsion of an injunction decree" from a prior case, the

royalty payments did not defeat justiciability. *Id.* at 365-66. The Court stressed that "the involuntary or coercive nature of the exaction" – *i.e.*, the injunction, which gave the counterclaimant no option but to pay the royalties – "*preserve[d] the right . . . to challenge the legality of the claim.*" *Id.* at 365 (emphasis added). In other words, *Altvater* found justiciability notwithstanding royalty payments only because the licensee did not have the option of stopping payment. Here, by contrast, MedImmune *chose* to pay royalties; it could have ceased paying royalties at any time to challenge the patent.

Similarly, MedImmune's suggestion that under this Court's decision in *Cardinal Chemical Co. v. Morton International, Inc.*, 508 U.S. 83 (1993), a plaintiff can invoke Declaratory Judgment Act jurisdiction "'[m]erely . . . to avoid the threat of a "scarecrow" patent'" is just wrong. Pet. at 10 (quoting *Cardinal Chem.*, 508 U.S. at 96). *Cardinal Chemical* involved a ripe dispute worthy of adjudication because in that case a patentee sued the defendant for infringement and the defendant asserted a declaratory judgment *counterclaim*. *Cardinal Chem.*, 508 U.S. at 95-96. Because there was plainly a live controversy between the parties, *Cardinal Chemical* does not inform the analysis here.[6] Indeed, subsequent decisions recognize that *Cardinal Chemical* did not alter well settled justiciability analysis in patent cases. *See, e.g.*, *Super Sack Mfg. v. Chase Packaging Corp.*, 57 F.3d 1054, 1060 (Fed. Cir. 1995) (rejecting notion that *Cardinal Chemical* "cut[s] [the] two-step justiciability analysis off at the pass" and concluding that the decision

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[6] *Bresnick v. U.S. Vitamin Corp.*, 139 F.2d 239 (2d Cir. 1943), which MedImmune cites for Judge Hand's reference to a "scarecrow" patent (Pet. at 10), is equally inapplicable because that case similarly involved an infringement suit by a patentee and did not address jurisdictional issues.

"does not revolutionize the justiciability of declaratory judgment actions attacking a patent's validity").

The Federal Circuit's application of the "reasonable apprehension" test in licensee cases like this one also does not present an overly broad and inflexible "absolute requirement" at odds with this Court's direction that Declaratory Judgment Act jurisdiction requires consideration of "all the circumstances." Pet. at 11 (citing *Md. Cas. Co.*, 312 U.S. at 273). The Federal Circuit merely recognized that a license, the essence of which is a covenant not to sue on the licensed patents, is in most instances inconsistent with a reasonable apprehension of litigation. *See Ortho Pharm. Corp. v. Genetics Inst.*, 52 F.3d 1026, 1031 (Fed. Cir. 1995) (a patent license is "a covenant by the patentee not to sue the licensee"). The Federal Circuit's observation reflects its understanding of the critical "circumstance" in this case: a covenant not to sue. Such a covenant typically *should* be dispositive. However, if a licensee can show what MedImmune could not – facts and circumstances demonstrating a reasonable apprehension of suit – declaratory judgment jurisprudence will not stand in its way. The Federal Circuit explicitly retained the "totality-of-the-circumstances test" (Pet. App. 7a-8a), preserving the flexibility needed to deal with unusual facts not present in this case.[7] To be sure, the Federal Circuit's decisions in *Gen-Probe* and subsequent cases, including this case, have drawn attention to the inherent tension between obtaining a patent license and then later claiming to have a reasonable

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[7] One can imagine, for example, a live dispute over a patent arising just before a license expired, but where the patent term still had some years to run. If the patent-holder threatened suit unless the licensee agreed to an extension, there very well could be an actionable controversy. *See, e.g., Hal Roach Studios, Inc. v. Richard Feiner & Co.*, 896 F.2d 1542 (9th Cir. 1990). Of course, a live dispute might also exist where the licensee withheld royalty payments, or violated some other express contractual provision.

fear of suit.[8] But the point itself is unassailable, and undeserving of this Court's review.

Here, the Federal Circuit correctly refused to hold that the desire to be released from the obligations of a license, without more, is enough to create a cognizable case or controversy between the parties. There is no conflict between the Federal Circuit's decision and this Court's precedent.

### B. The Federal Circuit's Decision Does Not Conflict With Circuit Court Precedent.

MedImmune cites an array of circuit court decisions, some involving licenses but others not, that it argues conflict with the decision below. None of MedImmune's cases rejects or even questions the reasonable apprehension of suit test applied in this case. Thus, none of the cases presents a conflict in legal standards. Of course, there are differing *outcomes*, but that will always be the case when a totality-of-the-circumstances test is applied to different facts. However, there is no disagreement among the circuits concerning the fundamental principle that Declaratory Judgment Act jurisdiction exists only if the plaintiff can show a "reasonable apprehension of suit" by the defendant.

#### 1. Non-License Cases

MedImmune's non-license cases merit little attention. Precisely because they do not involve licenses, these cases do not consider the key question of how a *covenant not to sue* affects justiciability. The Federal Circuit's reasoning in this case turns on the nature of a license, and is inherently

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[8] Cases applying *Gen-Probe* include *MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005), *petition for cert. filed*, 74 U.S.L.W. 3336 (U.S. Nov. 22, 2005) (No. 05-656), which concerns the same MedImmune practice at issue here.

confined to licenses – or, if one prefers, covenants not to sue generally.[9] Cases without this feature offer little value.

MedImmune mistakenly relies on such cases to contest the proposition "that there must be a material breach of the license contract in order to present a constitutional case or controversy." Pet. at 14-15. There are two problems with MedImmune's position. First, because those cases do not involve licenses, they could not possibly address that point. Second, the Federal Circuit did *not* hold that *all* licensees must breach to establish jurisdiction. Rather, the court held that a licensee, like every other declaratory judgment plaintiff, must identify *some* "actual controversy." In MedImmune's cited cases, in contrast to this case, the parties were committed to, or in some cases forced into, courses of conduct that made a breach by one party highly likely. *See, e.g.*, *Keener Oil & Gas Co. v. Consol. Gas Util. Corp.*, 190 F.2d 985, 988-90 (10th Cir. 1951) (the declaratory judgment plaintiff, a gas utility company, had no choice but to switch gas suppliers and the defendant, a pipeline operator, disputed its ability to do so); *Am. Mach. & Metals, Inc. v. De Bothezat Impeller Co.*, 166 F.2d 535, 536 (2d Cir. 1948) (actual controversy present where plaintiff expressed that it "desires and intends" to terminate the contract and continue manufacturing allegedly infringing products, and defendant "has led plaintiff to believe that upon termination of the contract defendant will sue plaintiff if it does not cease manufacture and sale" of the products (internal quotation marks and citation omitted)); *Venator Group Specialty, Inc. v. Matthew/Muniot Family, LLC*, 322 F.3d 835, 840-41 (5th Cir. 2003) (conflict over the validity of a lease provision that

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[9] MedImmune is therefore wrong when it claims that "[t]here is no way to confine [the Federal Circuit's] reasoning to a single subset of contracts, patent licenses." Pet. at 11. There is no reason whatsoever to think that courts are unable to distinguish between the effects of an uncontested covenant not to sue and other, ordinary kinds of contracts when determining justiciability.

required property to be restored to pre-lease condition at end of lease was "very likely" because "the lease term *will* end" and adjoining property would be rendered unmarketable were plaintiff's position sustained). Cases concerning "very likely" breaches are simply not helpful.[10]

**2. License Cases**

Most of the pre-Federal Circuit patent cases MedImmune cites are distinguishable because an "actual controversy" was apparent. In *Precision Shooting Equipment Co. v. Allen*, 646 F.2d 313 (7th Cir. 1981), the licensee tendered its license payments to the court rather than to the licensor. *Id.* at 314, 318. The licensee thus was not in "good standing," and the parties had a sufficient conflict to create a justiciable controversy. *See id.* at 318 ("if not for the injunction it is obvious [the declaratory judgment defendant] would seek to terminate the license because it does not have possession of the escrowed royalties"). In *Societe de Conditionnement v. Hunter Engineering Co.*, 655 F.2d 938 (9th Cir. 1981), the plaintiff was not a licensee, was not immunized by a contractual covenant not to sue, and therefore could demonstrate a real and concrete fear of suit if it continued to manufacture the allegedly infringing product. *Id.* at 944-45. In *American Sterilizer Co. v. Sybron Corp.*, 526 F.2d 542 (3d Cir. 1975), the licensee had refused to pay

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[10] MedImmune's reliance on the remaining non-license cases is equally puzzling. In each case, there was either a change in circumstances, or one of the parties had created an actual prospect of litigation or breach of contract. *See, e.g., NUCOR Corp. v. Aceros y Maquilas de Occidente, S.A. de C.V.*, 28 F.3d 572, 575, 578 (7th Cir. 1994) (declaratory judgment defendant "demanded payment of $685,000 in damages within 60 days" and had "clearly threatened suit"). None of those factors is present here.

royalties on the grounds that its product did not infringe the patent.[11] *Id.* at 544.

Similarly distinguishable are the non-patent license cases MedImmune cites. Pet. at 14. These cases each involved additional facts that, under the totality of the circumstances, supported a reasonable apprehension of suit on the part of the declaratory judgment plaintiff. In *National Car Rental System, Inc. v. Computer Associates International, Inc.*, 991 F.2d 426 (8th Cir. 1993), for example, the copyright licensee sued under the Declaratory Judgment Act after the licensor had threatened to sue for allegedly breaching the scope of the license. *Id.* at 428. In *S.O.S., Inc. v. Payday, Inc.*, 886 F.2d 1081 (9th Cir. 1989), the licensee raised a declaratory judgment *counterclaim* after the licensor had sued the licensee for copyright infringement alleging a breach of the license. *Id.* at 1084-85. In *Hal Roach Studios, Inc. v. Richard Feiner & Co.*, 896 F.2d 1542 (9th Cir. 1990), the copyright licensee had explicitly threatened to continue using the copyrighted material after expiration of the license, which was imminent. *Id.* at 1556. The Ninth Circuit applied the "reasonable apprehension" test and concluded that under the totality of the circumstances there was a sufficient present controversy to support jurisdiction. *Id.* at 1555-56.

The only case MedImmune cites that could arguably be read as disagreeing with the Federal Circuit's decision is the 1977 decision of the Second Circuit in *Warner-Jenkinson Co. v. Allied Chemical Corp.*, 567 F.2d 184 (2d Cir. 1977). It is questionable whether *Warner-Jenkinson* is followed on this issue even in the Second Circuit, which routinely applies

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[11] Furthermore, like several of the cases MedImmune cites, *American Sterilizer* does not even discuss this jurisdiction issue and therefore cannot be cited for the proposition that jurisdiction was present. *See, e.g., Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 91 (1998) ("drive by" jurisdictional rulings are entitled to no precedential weight).

the "reasonable apprehension of suit" test. *See, e.g., Starter Corp. v. Converse, Inc.*, 84 F.3d 592, 595 (2d Cir. 1996) (declaratory judgment plaintiff must have a "real and reasonable apprehension of litigation" and "must have engaged in a course of conduct which brought it into adversarial conflict with the declaratory defendant"); *Matthew Bender & Co. v. West Publ'g Co.*, 240 F.3d 116, 119 (2d Cir. 2001) (discussing the district court's appropriate application of the reasonable apprehension test for determining declaratory judgment jurisdiction in a copyright case). In *Atlantic Richfield Co. v. Alcan Aluminum Holdings Ltd.*, 12 F. Supp. 2d 460 (S.D.N.Y. 1998), for example, a district court applying Second Circuit law concluded that a declaratory judgment case was not justiciable because the plaintiff only sought a declaration to assure the availability of breaching a contract as an option "if economic analysis shows that it would be the most profitable course." *Id.* at 460-61. Such relief, of course, is precisely what MedImmune seeks here – a declaration that *if* it chose to breach its license it would have a valid defense to any subsequent infringement lawsuit Genentech *might* bring.

## III. THE DECISION BELOW HARMONIZES WITH *LEAR*.

The crux of MedImmune's argument is its flawed construction of *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969). Yet the petition does not allege any actual conflict with *Lear*, and with good reason. *Lear* had nothing to do with the case or controversy requirement under Article III and the Declaratory Judgment Act, and it arose in a context in which a justiciable controversy was clearly present. *Lear* addressed whether a licensee, *sued by its licensor* for non-payment of royalties, could defend the suit by attacking the patent's validity. *Id.* at 660, 670-71. Prior cases had held that licensees were estopped, as a matter of substantive law, from denying the validity of the patent in any litigation context.

*Id.* at 663-64. *Lear* eliminated that "licensee estoppel" doctrine and leveled the playing field between licensors and licensees by permitting a licensee *who had stopped paying royalties* to defend a suit by the licensor for non-payment on the grounds that the licensed patent was invalid.

*Lear* thus stands for a point of substantive patent law: licensing a patent does not concede its validity and forever bar the licensee from attacking the patent's validity. It is an important point, but it has nothing to do with Article III jurisdiction. As the Federal Circuit pointed out over twenty years ago, "*Lear* . . . left unresolved the question when a federal court has jurisdiction of a licensee's claim of patent invalidity." *C.R. Bard, Inc. v. Schwartz*, 716 F.2d 874, 878 (Fed. Cir. 1983).

MedImmune nevertheless claims that the decision below "adopted a policy at odds with the policy of the patent laws as declared by this Court" in *Lear*. Pet. at 19. It did no such thing. The Federal Circuit's decision in this case conflicts with *Lear* only if one reads *Lear*'s general observations about the public interest in challenging weak or invalid patents to *require* giving licensees unfettered rights to commence litigation at any time, irrespective of whether there is an Article III controversy. Nothing remotely like that is found in the Court's decision. Indeed, a key principle for the *Lear* Court was balance between the rights of the licensor and licensee. The "licensee estoppel" doctrine plainly favored licensors by forever estopping licensees from challenging the validity of a patent – even if they ceased paying royalties under the license. This Court sought to "balance the claims of promisor and promisee in accord with the requirements of good faith." *Lear*, 395 U.S. at 670. Thus, if the licensor sued under the license, it was only fair that the licensee could assert all relevant defenses, including invalidity.

MedImmune's theory would upset that balance by skewing it overwhelmingly in favor of licensees. Under

MedImmune's view, a licensee can negotiate a patent license on the best available economic terms – terms that cap the licensee's risk and inherently reflect any existing uncertainty about the patent's validity[12] – and then, the next day, sue to invalidate the same patent. The licensor has no parallel right, for as long as the licensee continues to pay royalties, the licensee could bind the licensor's hands and prevent it from terminating the license. This would not "balance the claims of promisor and promisee in accord with the requirements of good faith," *Lear*, 395 U.S. at 670; it would give licensees an undeserved second bite at the apple with everything to gain and nothing to lose. Neither *Lear* nor any other holding of this Court supports such a disproportionate imposition of risk upon the patent-holder.

It is, in any event, impossible for the Congress or a decision of this Court to have created a policy-based exception to Article III's "case or controversy" requirement. That is a fundamental limitation on the constitutional power of the federal courts, designed to protect the separation of powers and the integrity of the judicial role. Congress could not, for any policy reason, authorize the federal courts to hear a hypothetical controversy. This Court has never created a policy-based exception to the case or controversy requirement. And if this were to be the first such instance, there would be no way to confine the exception MedImmune seeks just to patent cases. The message to the legal community would be that with a good enough policy argument one indeed may, as Judge Posner put it in *Crowley*

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[12] It is widely recognized that patent licenses implicitly take into account the licensing parties' views as to the validity of the patents, whether they are infringed, and whether there are work-arounds. *See* Carl Shapiro, *Antitrust Limits to Patent Settlements*, 34 RAND J. Econ. 391, 392 (2003) ("Virtually every patent license can be viewed as a settlement of a patent dispute: the royalty rate presumably reflects the two parties' strengths or weaknesses in patent litigation in conjunction with the licensee's ability to invent around the patent.").

*Cutlery*, come to federal court simply "for advice on the legality of a proposed course of action." *Crowley Cutlery*, 849 F.2d at 276. Neither policy arguments generally nor anything found in *Lear* can justify such a radical change in settled Article III jurisprudence.

## IV. THE FEDERAL CIRCUIT'S DECISION RAISES NO ISSUES OF NATIONAL IMPORTANCE AND DOES NOT THREATEN THE PACE OF INNOVATION IN MEDICAL PRODUCTS.

MedImmune closes its petition with the doomsday prediction that, unless patent licensees are allowed to file suit for what would effectively be advisory opinions, the pace of innovation in "new medical drugs and treatments" will be inhibited. Pet. at 19. This policy argument is irrelevant for the reasons just discussed. In addition, it is wholly lacking in substance.

MedImmune's assertion that the public can only be protected from invalid patents by allowing licensees in good standing to sue their licensors (or allowing non-licensees who have never been threatened with suit by a patentee to sue, for that matter) – is wrong. There are at least three different ways the validity of a patent may be tested (and through one of these procedures the '415 patent is currently under review). First, a licensee such as MedImmune may refuse to pay or cease paying royalties and, as in *Lear*, induce an infringement suit. Second, anyone who is not licensed and is threatened with suit may challenge the patent under the Declaratory Judgment Act. Third, any member of the public, even a patent licensee in good standing, may seek reexamination of a patent by the PTO at any time.[13] In fact,

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[13] The federal patent statutes permit anyone to ask the PTO to reconsider the validity of an issued patent based on prior art. 35 U.S.C. §§ 302, 311(b); *see also id.* § 301. The patent statutes provide for two different types of reexamination. For patents issuing from an application

the '415 patent currently is being reexamined. Indeed, this ongoing PTO reexamination has the potential to moot the issues that MedImmune is asking to litigate, which is a further reason to deny review.

Given the various options for challenging the validity of patents, the courts need not, under the guise of protecting the public, disregard the constitutional requirement of an actual controversy and allow licensees who are immune from suit to challenge the validity of licensed patents in court. The patent system is more robust than that, as the facts of this case prove.

MedImmune's proposed rule would also make it difficult, if not impossible, for parties to a licensing negotiation to allocate risk. The agreed royalty rate in a license agreement reflects the perceived strength of the patent (among other factors). But if the licensor has no protection from an invalidity attack as soon as the license is signed, risk cannot be allocated. It makes no sense to think that impairing contractual certainty in this manner will promote innovation. The opposite is more likely correct.

MedImmune also asserts that it was the victim of an "all too common" package licensing strategy in which a

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filed on or after November 29, 1999, the requesting party may request either an *inter partes* or an *ex parte* reexamination. *See id.* § 311; 37 C.F.R. § 1.913. If the PTO grants an *inter partes* reexamination request, the third party requesting reexamination retains the ability to remain substantively involved throughout the reexamination process. The requesting party may continue to make arguments about validity throughout the reexamination process, and may appeal any outcome in favor of validity to the Board of Patent Appeals and Interferences and then to the Federal Circuit. *See* 35 U.S.C. §§ 306, 314(b), 315. If the PTO grants an *ex parte* reexamination request, the requesting party is not substantively involved in the reexamination process. *Ex parte* reexamination has been a part of the patent statute since 1980. For the '415 patent, the PTO has granted an *ex parte* request for reexamination, and the proceeding is currently ongoing.

putatively "bad" patent (the '415 patent) was licensed as part of a "bundle" with other patents. Pet. at 19-20. That argument is wrong. MedImmune, "for reasons of convenience," expressly elected not to license the '415 patent alone. C.A.A. 3585. Moreover, MedImmune has no products covered by the '567 patent it licensed along with the '415 patent, and thus could not fear losing license rights to the '567 patent by challenging the '415 patent. *See* C.A.A. 3312, 3316-17. At any rate, the answer to this supposed issue lies in the parties' license negotiations, not a wholesale revision of Article III jurisprudence. A licensee may negotiate for the right to challenge one licensed patent without risking a breach of other patent license rights. *See, e.g., Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1368-69 (Fed. Cir. 2004) (patent licensee stopped paying royalties on one licensed product; all parties agreed the license agreement was still in effect as to other licensed product), *cert. granted on other grounds*, 126 S. Ct. 601 (2005). This solution is at least as "common" as MedImmune contends bundling is (Pet. at 19), and does not require this Court to change Article III doctrine to address MedImmune's policy concerns.

## CONCLUSION

Sound policy does not justify limitless encouragement of no-risk, roll-the-dice lawsuits seeking to invalidate licensed patents. The Federal Circuit's unexceptional application of the case or controversy requirement correctly strikes the right balance: allow licensees, like any other litigant, to seek declaratory relief when they have a reasonable apprehension of suit; but forbid licensees, like any other litigant, from seeking declaratory relief when they lack such apprehension.

The petition for a writ of certiorari should be denied.

Respectfully submitted,

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December 27, 2005

No. 05-608

IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

v.

GENENTECH, INC., *et al.*,

*Respondents.*

**On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## REPLY TO BRIEF IN OPPOSITION


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IN THE

# Supreme Court of the United States

No. 05-608

MEDIMMUNE, INC.,

*Petitioner,*

v.

GENENTECH, INC., *et al.*,

*Respondents.*

**On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## REPLY TO BRIEF IN OPPOSITION

The Federal Circuit after *Gen-Probe*[1] now requires that patent licensees commit a material breach of contract before they can sue under the Declaratory Judgment Act, 28 U.S.C. § 2201, to challenge validity, enforceability, or infringement. Unless material breach has occurred, the Federal Circuit now banishes

[1] *Gen-Probe Inc.* v. *Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir.), *pet'n for cert. dismissed*, 543 U.S. 941 (2004). *Gen-Probe* and the decisions following it contradict prior Federal Circuit law. See *C.R. Bard, Inc.* v. *Schwartz*, 716 F.2d 874, 882 (Fed. Cir. 1983) ("we hold that a patent licensee may bring a federal declaratory judgment action . . . without prior termination of the license"); see also *Gen-Probe Inc.* v. *Vysis*, No. 99-CV-2668H (S.D. Cal. Mar. 12, 2002) ("It is settled law that an effective license between the parties does not preclude federal question jurisdiction over a licensee's declaratory judgment action."), *rev'd*, 359 F.3d 1376 (Fed. Cir.), *pet'n for cert. dismissed*, 543 U.S. 941 (2004) (reprinted in Petition for Certiorari, *Gen-Probe Inc.* v. *Vysis, Inc.*, No. 04-260, at 25a).

such disputes from the avenue of relief Congress provided in the Declaratory Judgment Act. Certiorari is appropriate because the Federal Circuit has acted contrary to the established understanding of Article III and the Declaratory Judgment Act, and also contrary to the policy of the patent laws as held in *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969)..

### A. "Reasonable Apprehension of Suit."

The Declaratory Judgment Act extends to the limits of Article III. *Ashwander* v. *TVA*, 297 U.S. 288, 325 (1936); see Pet. Cert. 11 n.8. The simple jurisdictional requirement is that there be a dispute as to legal rights that is—as here—"definite and concrete." *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227, 242 (1937).

> "The sole requirement for jurisdiction under the Act is that the conflict be real and immediate, i.e., that there be a true, actual 'controversy' required by the Act."

*Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83, 96 (1993), quoting *Arrowhead Indus. Water, Inc.* v. *Ecolochem, Inc.*, 846 F.2d 731, 735 (Fed. Cir. 1988).[2]

That constitutional requirement was fully satisfied in this case. Petitioner sought resolution of "a concrete case admitting of an immediate and definitive determination of the legal rights of the parties in an adversary proceeding upon the facts alleged." *Aetna*, 300 U.S. at 241. Respondents have never wavered in asserting that the licensed patent is valid and infringed by petitioner's Synagis®; and petitioner equally has never wavered in disputing those assertions. The fact that petitioner has not in addition committed a material breach does not convert this mature and concrete dispute into what respondents call "a hypothetical" set of facts. Br. Opp. 10, quoting *Aetna*, 300 U.S. at 241.

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[2] Of course no one disputes the familiar proposition, see Br. Opp. 10-11, that if there is no actual controversy, federal courts may not issue advisory opinions as to purely hypothetical situations.

The "reasonable apprehension of suit" formulation, which courts have applied in varying situations, is not an exclusive determinant of Article III jurisdiction in every instance, nor does it overrule this Court's decisions going back to *Aetna*. It is simply a sometimes convenient proxy for the Article III and DJA requirement of "actual controversy." As the First Circuit has explained, "reasonable apprehension of suit"

> "is not the only way to establish the existence of a case for purposes of Article III."

*Sallen* v. *Corinthians Licenciamentos LTDA*, 273 F.3d 14, 25 (1st Cir. 2001). An actual and concrete dispute as to legal rights between adverse parties satisfies Article III and the Declaratory Judgment Act, whether or not described as "apprehension of suit." *Id.*

The issue presented in the petition is not the phrase "reasonable apprehension of suit." Rather, it is that the Federal Circuit now has *redefined* "reasonable apprehension of suit" —and with it Article III and the statutory term "actual controversy"—to require absolutely that before a patent licensee can seek a declaratory judgment, it must place itself in material breach—and at risk of treble damages, penalties, and injunction—contrary to the Declaratory Judgment Act's central purpose. P.C.A. 5a-6a, citing *Gen-Probe*. But this Court held long ago that a patent licensee should not have to choose between paying "the heavy hand of . . . tribute" or

> "risk[ing] not only actual but treble damages in infringement suits. . . . It was the function of the Declaratory Judgments Act to afford relief against such peril and insecurity."

*Altvater* v. *Freeman*, 319 U.S. 359, 365 (1943).[3]

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[3] Only by assuming the validity of *Gen-Probe*'s new definition could the Federal Circuit say that "MedImmune concedes that it is free of apprehension of suit." P.C.A. 4a, cited at Br. Opp. 3. MedImmune expressly asserted apprehension that it would be sued for treble damages

## B. Conflict With Other Circuits.

The petition discussed a number of decisions in other Circuits that place the Federal Circuit's constitutional interpretation diametrically at odds with the application of Article III and the Declaratory Judgment Act in other courts of appeals. Pet. Cert. 14-16. Several of those decisions the Brief in Opposition does not mention.[4] Others it brushes aside with the comment that "[c]ases concerning 'very likely' breaches are simply not helpful." Br. Opp. 18.

To play down the conflict with other Circuits, respondents rely instead on a long string of opinions that have used the phrase "reasonable apprehension of suit." Br. Opp. 8-9 n.4. But none of the cases respondents cite used the phrase "reasonable apprehension of suit" to mean what the Federal Circuit redefined it to mean in *Gen-Probe* and here: material breach as a precondition to suit. Indeed, not a single one involved an enforceable patent license, or a license of any other kind. Most were ordinary determinations of whether a threat of infringement, not involving a license, was immediate enough or too speculative to be an "actual controversy." Many antedated the Federal Circuit and further confirm, as the petition already has demonstrated, that the law was firmly established that licensees were not required to commit material breach before seeking declaratory relief. Pet. Cert. 13-14.

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and onerous penalties if it ceased to pay royalties—which was what the Federal Circuit then ruled under *Gen-Probe* was no longer jurisdictionally sufficient.

[4] *E.g.*, *Doody* v. *Ameriquest Mortgage Co.*, 242 F.3d 286, 288 (5th Cir. 2001) (DJA authorizes suits "before the dispute grows into a contract violation"); *Continental Cas. Co.* v. *Coastal Sav. Bank*, 977 F.2d 734, 738 (2d Cir. 1992) (DJA "intended to avoid precisely the 'accrual of avoidable damages to one not certain of his rights'"); *ACandS, Inc.* v. *Aetna Cas. & Surety Co.*, 666 F.2d 819, 823 (3d Cir. 1981) (quoting *Continental*); see Pet. Cert. 14-16.

Not only do the opinions respondents cite provide no support for the Federal Circuit rule: several are in fact antithetical to it. In *National Basketball Ass'n* v. *SDC Basketball Club, Inc.*, 815 F.2d 562 (9th Cir. 1987), cited Br. Opp. 9 n.4, the court held that a party to a joint venture agreement could bring an action under the Declaratory Judgment Act without first exposing itself to risk of liability:

> "The . . . alternative formulation of case and controversy would force the NBA to impose a fine or sanction on the Clippers before an action could accrue. *This is the type of Damoclean threat that the Declaratory Judgment Act is designed to avoid.* . . . Since the NBA's 'real and reasonable apprehension' . . . was that any action on the Clippers' move could result in antitrust liability, the case is justiciable."

*Id.* at 566 (emphasis supplied). Similarly, in *GTE Directories Pub. Corp.* v. *Trimen America, Inc.*, 67 F.3d 1563 (11th Cir. 1995), the court rejected a supposed requirement to risk or incur potential liability:

> "The practical effect of finding no case or controversy in the instant case would be to force GTEDPC to contact Trimen's clients thereby subjecting itself to potential liability before allowing it to receive a declaratory judgment. GTEDPC is not required to take such action for an actual case or controversy to exist."

*Id.* at 1568.

*Crowley Cutlery Co.* v. *United States*, 849 F.2d 273, 276 (7th Cir. 1988), quoted at Br. Opp. 11, required simply that there be "an existing legal dispute"—as there is here. In fact, the court's relevant jurisdictional holding (dismissing on other grounds) was that the plaintiff's stated fear of prosecution for importing switchblade knives was sufficient to "satisfy the requirements of Article III." *Id.*

Presented with the exact issue raised here, the Second Circuit held that licensees need not withhold royalty payments, because "such repudiation of the licensing agreement should not be precondition to suit." *Warner-Jenkinson Co.* v. *Allied Chem. Corp.*, 567 F.2d 184, 187 (2d Cir. 1977) (citing "most courts who have considered the issue"). Respondents acknowledge *Warner-Jenkinson* as "arguably . . . disagreeing with the Federal Circuit's decision." Br. Opp. 19.[5] And in *Precision Shooting Equip. Co.* v. *Allen*, 646 F.2d 313 (7th Cir.), *cert. denied*, 454 U.S. 964 (1981), the Seventh Circuit held sufficient under Article III that the licensee alleged "a reasonable apprehension that the patentee will bring an infringement suit against him *if* there is non-compliance with the license." *Id.* at 318 (emphasis supplied); see Pet. Cert. 13. Those jurisdictional principles apply no less in the regional Circuits today. *E.g.*, *Starter Corp.* v. *Converse, Inc.*, 84 F.3d 592, 595 (2d Cir. 1996), cited at Br. Opp. 20 (jurisdiction satisfied based on communication of "intent" "to bring an infringement suit should Starter engage in the sale.").

### C. The Federal Circuit's Jurisdictional Rule.

*Gen-Probe* has declared an absolute jurisdictional rule that hereafter the

> "license, unless materially breached, *obliterated any reasonable apprehension of a lawsuit.*"

359 F.3d at 1381 (emphasis supplied). As the District Court pointedly recognized, until *Gen-Probe*,

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[5] Respondents assert that *Warner-Jenkinson* somehow was challenged *sub silentio* by decisions using the phrase "reasonable apprehension of suit." Br. Opp. 18-19. That is not correct. Moreover, a plaintiff "need not prove that [the defendant] expressly has threatened to take legal action." *Interdynamics, Inc.* v. *Wolf*, 698 F.2d 157, 167 (3d Cir. 1982), cited at Br. Opp. 9 n.4.

> "In the past, the 'actual controversy' requirement has not been interpreted by precluding a licensee from challenging a patent it licenses."

P.C.A. 24a. The Federal Circuit's absolute rule also contradicts this Court:

> "The difference between an abstract question and a 'controversy' contemplated by the Declaratory Judgment Act is necessarily one of degree, and *it would be difficult*, if it would be possible, *to fashion a precise test* for determining in every case whether there is such a controversy."

*Maryland Cas. Co.* v. *Pacific Coal & Oil Co.*, 312 U.S. 270, 273 (1941) (emphasis supplied).

Respondents at one point pretend that the Federal Circuit nevertheless "retained the totality-of-the-circumstances test." Br. Opp. 15. That is plainly not so in any meaningful sense. What the Federal Circuit unambiguously held, both in *Gen-Probe* and here, was that "the jurisdictional requirements of a declaratory action are not met when royalties are fully paid to the licensor and there is no ground on which the licensor can cancel the license or sue for infringement." P.C.A. 6a. The Federal Circuit described its mechanical *Gen-Probe* rule as its "synthesis of the totality-of-the-circumstances test for determining whether there is a justiciable controversy." P.C.A. 7a-8a. Citing *Gen-Probe*, the Federal Circuit reiterated that without breach "there is no defaulting licensee and *no possibility of suit*." P.C.A. 6a (emphasis supplied).

On that basis the Federal Circuit in the present case held that "as a licensee in good standing" petitioner "cannot bring a declaratory action to challenge the patent under which it is licensed" because there is "no justiciable controversy." P.C.A. 4a-5a. There has not been a Federal Circuit case since *Gen-Probe* that has held otherwise. The Federal Circuit has followed *Gen-Probe* four times and declined four petitions

for rehearing *en banc*,[6] and the 94 district courts in patent cases are obediently applying, however skeptically,[7] this new Article III jurisdictional rule.

### D. *Lear, Inc.* v. *Adkins.*

For several years, the Federal Circuit has been issuing decisions critical of this Court's holding in *Lear*, and seeking every possible way to escape it. See, *e.g.*, *Studiengesellschaft Kohle, m.b.H.* v. *Shell Oil Co.*, 112 F.3d 1561, 1567 (Fed. Cir.) (*Lear* sounds "tones that echo from a past era"), *cert. denied*, 522 U.S. 966 (1997); *Gen-Probe*, 359 F.3d at 1381 ("In several instances, this court has declined to apply the *Lear* doctrine."); cases cited at Pet. Cert. 17-18.

With *Gen-Probe* and the present case, the Federal Circuit now has effectively done away with *Lear* completely for licensees not in material breach. Being unable frontally to overturn this Court's *Lear* holding under the patent laws—which was reiterated in *Cardinal Chem. Co.*, 508 U.S. at 96, 100—it has achieved nearly the same result by an unprecedented rereading of Article III and the Declaratory Judgment Act. Moreover, by invoking the Constitution, it has placed its revival of licensee estoppel beyond the power of

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[6] In *Gen-Probe*; in *MedImmune, Inc.* v. *Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005), *pet'n for cert. pending* (No. 05-656); in *Metabolite Labs., Inc.* v. *Laboratory Corp. of America Holdings*, 370 F.3d 1354, 1369 (Fed. Cir. 2004), *cert. granted on another question*, 126 S. Ct. 601 (2005) (No. 04-607); and in *Teva Pharmaceuticals USA, Inc.* v. *Pfizer, Inc.*, 405 F.3d 990 (Fed. Cir.) (three judges dissenting), *cert. denied*, 126 S. Ct. 473 (2005).

[7] *E.g.*, P.C.A. 31a ("serious misgivings"), noting that the Federal Circuit now

> "forces licensees to take tremendous risk to challenge a patent, one that some with valid claims will likely be unwilling to take."

P.C.A. 30a.

Congress to correct. The only body in a position effectively to do so is now this Court.

## CONCLUSION

For the reasons stated herein and in the petition, certiorari should be granted.[8]

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January 12, 2006

[8] Respondents note that some patents can receive narrow reexamination by the U.S. Patent and Trademark Office pursuant to 35 U.S.C. §§ 302 and 311. Br. Opp. 23-24. That very limited procedure, however, is not nearly equivalent to challenge of a patent in an adversarial judicial proceeding, and is limited to prior printed publications and patents. 35 U.S.C. § 302. Petitioner's challenges—based on inequitable conduct, fraud on the Patent Office, lack of adequate support in the patent for the invention, non-infringement, and other fundamental violations—cannot be raised in such a proceeding.

(23)

No. 05-608

FILED
MAY 17 2006
OFFICE OF THE CLERK
SUPREME COURT, U.S.

IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,
*Petitioner*,

v.

GENENTECH, INC., *et al.*,
*Respondents.*

**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## JOINT APPENDIX
## VOLUME I

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**PETITION FOR CERTIORARI FILED NOVEMBER 10, 2005**
**CERTIORARI GRANTED FEBRUARY 21, 2006**

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NOTICE

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Certificates of service whenever appended to documents appearing herein have been omitted in printing. Where redactions have been made, they are noted by ellipses or otherwise.

U.S. DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
(Western Division - Los Angeles)

---

CIVIL DOCKET FOR CASE #: 2:03-cv-02567-MRP-CT

MEDIMMUNE INC.,

*Plaintiff,*

v.

GENENTECH INC., *et al.*,

*Defendants.*

---

Assigned to: Judge Mariana R. Pfaelzer
Referred to: Discovery Carolyn Turchin
Demand: $0
Cause: 28:1338 Patent Infringement
Date Filed: 04/11/2003
Jury Demand: Both
Nature of Suit: 830 Patent
Jurisdiction: Federal Question

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | * * * * |
| 04/11/2003 | 1 | COMPLAINT filed Summons(es) 20 days issued referred to Discovery Carolyn Turchin (rrey) (Entered: 04/14/2003) |
| | | * * * * |
| 05/29/2003 | 16 | ORDER TRANSFERRING ACTION Under Section 3.1 of General Order 224 Case transferred from Judge Terry J. Hatter to Judge Mariana R. Pfaelzer for all further proceedings. The case number will now reflect the initials of the transferee Judge [ CV 03-3567 MRP (CTx)] (cc: all counsel) (m) (Entered: 05/29/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | * * * * |
| 06/04/2003 | 20 | ANSWER filed by defendant Celltech R&D Ltd to complaint [1-1]; jury demand (el) (Entered: 06/05/2003) |
| 06/04/2003 | 21 | NOTICE OF MOTION AND MOTION by defendant Genentech Inc to dismiss the third and eleventh causes of action ; motion hearing set for 10:00 7/21/03; Memorandum of Points and Authorities in support (el) (Entered: 06/05/2003) |
| 06/04/2003 | 22 | NOTICE OF MOTION AND MOTION by defendant City of Hope Natl for joinder in motion to dismiss the third cause of action [21-1] ; motion hearing set for 10:00 7/21/03 (el) (Entered: 06/05/2003) |
| | | * * * * |
| 6/05/2003 | 24 | NOTICE OF ERRATA by defendant Genentech Inc correcting motion to dismiss the third and eleventh causes of action [21-1], filed on 6/4/03 (el) (Entered: 06/06/2003) |
| | | * * * * |
| 06/23/2003 | 32 | STIPULATION and ORDER by Judge Mariana R. Pfaelzer that the hearing on motion to dismiss the third and eleventh causes of action [21-1] shall be continued to 10:00 7/21/03; any opposition to the Motion to dismiss shall be filed 21 days before the hearing date. Any reply in support shall be filed seven (7) days before the hearing date (el) (Entered: 06/25/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 07/14/2003 | 33 | OPPOSITION by plaintiff Medimmune Inc to motion to dismiss the third and eleventh causes of action [21-1] (el) (Entered: 07/15/2003) |
| | | * * * * |
| 07/28/2003 | 35 | REPLY MEMORDUM OF POINTS AND AUTHORITIES by defendant Genentech Inc insupport of motion to dismiss the third and eleventh causes of action [21-1] (el) (Entered: 07/29/2003) |
| 07/28/2003 | 36 | REQUEST by defendant Genentech Inc for Judicial Notice re motion to dismiss the third and eleventh causes of action [21-1]; Lodged proposed order (el) (Entered: 07/29/2003) |
| 07/28/2003 | 37 | DECLARATION of Susan L Friedman in support by defendant Genentech Inc of request for judicial notice in support of reply memorandum for motion to dismiss the third and eleventh causes of action [21-1] (el) (Entered: 07/29/2003) |
| | | * * * * |
| 08/04/2003 | 39 | MINUTES before Judge Mariana R. Pfaelzer: Defendant's motion to dismiss the third and eleventh causes of action [21-1]; joined by City of Hope [21-1] [22-1]. Court GRANTS the motion to dismiss as to the 3rd cause of action with leave until 08/13/03, to amend. Court GRANTS the motion to dismiss as to the 11th cause of action without leave to amend. The parties shall submit their Rule 26() Report no later |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | than 08/08/03, and shall give notice of a hearing date and time for the Rule 26(f) scheduling conference in the report. CR: Lisa Gonzales (jp) (Entered: 08/04/2003) |
| 08/08/2003 | 40 | JOINT RULE 26 DISCOVERY PLAN filed; est length of trial 3-6 weeks (el) (Entered: 08/11/2003) |
| 08/11/2003 | 41 | ORDER by Judge Mariana R. Pfaelzer that the motion to dismiss the third and eleventh causes of action [21-1] is GRANTED as to the Third Cause of action, and plaintiff MedImmune has until 8/13/03 to file and serve a First Amended Complaint. The motion is GRANTED as to the Eleventh cause of action without leave to amend. (el) (Entered: 08/12/2003) |
| 08/13/2003 | 42 | FIRST AMENDED COMPLAINT [1-1] by plaintiff Medimmune Inc; jury demand. Summons not issued (el) (Entered: 08/14/2003) |
| 08/22/2003 | 43 | RECEIPT OF TRANSCRIPT of proceedings for the following date(s): 08/04/03 (Re:), CR: Lisa M. Gonzalez. (wdc) (Entered: 08/25/2003) |
| | | * * * * |
| 09/02/2003 | 44 | ANSWER filed by defendant Celltech R&D Ltd to First amended complaint [42-1], jury demand (el) (Entered: 09/03/2003) |
| 09/02/2003 | 45 | ANSWER filed by defendant City of Hope National Medical Center's to First amended complaint [42-1]; jury demand (el) (Entered: 09/04/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 09/02/2003 | 46 | ANSWER filed by defendant Genentech Inc to First amended complaint [42-1]; jury demand (el) (Entered: 09/04/2003) |
| 09/02/2003 | 47 | SCHEDULING CONFERENCE STATEMENT by defendant Genentech Inc in accordance with the parties' agreement and athe Joint Rule 26(f) Report [40-1]; addressing bifurcation issues in advance of the 9/8/03 Scheduling Conference (el) (Entered: 09/04/2003) |
| 09/02/2003 | 48 | SUBMISSION regarding Bifurcation and Scheduling by defendant Celltech R&D Ltd (el) (Entered: 09/04/2003) |
| 09/02/2003 | 49 | MEMORANDUM IN SUPPORT OF ITS PROPOSED DISCOVERY SCHEDULE AND IN OPPOSITION to defendants' requests to bifurcate or stay discovery on "Antitrust" issues by plaintiff Medimmune Inc (el) (Entered: 09/04/2003) |
| 09/02/2003 | 50 | DECLARATION of Jeffrey R Witham in support of plaintiff Medimmune Inc's proposed discovery schedule and in Opposition to defendants' requests to bifurcate or stay discovery on "Antitrust" issues (el) (Entered: 09/04/2003) |
| 09/08/2003 | 51 | MINUTES: Scheduling/Status Conference hearing held. Court and counsel schedule a telephone conference call for Monday, 12:00 9/15/03 , with Mr Kurzwiel, plaintiffs' counsel, arranging this call. Counsel are instructed to prepare a revised stipulated schedule confirming the pretrial and trial |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | dates by Judge Mariana R. Pfaelzer CR: Margaret Babykin (el) (Entered: 09/16/2003) |
| 09/15/2003 | 53 | MINUTES: Conference call held . Court will issue a scheduling order a a later date by Judge Mariana R. Pfaelzer CR: None Present (pj) (Entered: 09/17/2003) |
| 09/16/2003 | 52 | SCHEDULING ORDER: The parties adhere to the following scheduling order by Judge Mariana R. Pfaelzer (pj) (Entered: 09/17/2003) |
| 09/22/2003 | 54 | AMENDED ANSWER [44-1] by defendant Celltech R&D Ltd to First Amended Complaint; jury demand (el) (Entered: 09/23/2003) |
| 09/30/2003 | 55 | NOTICE OF MOTION AND MOTION by defendant Celltech R&D Ltd for judgment on the pleadings ; motion hearing set for 10:00 10/20/03 (el) (Entered: 10/01/2003) |
| 09/30/2003 | 56 | NOTICE OF motion for judgment on the pleadings [55-1] filed by defendant Celltech R&D Ltd (el) (Entered: 10/01/2003) |
| 09/30/2003 | 57 | REQUEST by defendant Celltech R&D Ltd for Judicial Notice re motion for judgment on the pleadings [55-1] (el) (Entered: 10/01/2003) |
| 09/30/2003 | 58 | DECLARATION of Jason A Carotty in support by defendant Celltech R&D Ltd of motion for judgment on the pleadings [55-1] (el) (Entered: 10/01/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 10/06/2003 | 59 | STIPULATION and ORDER by Judge Mariana R. Pfaelzer that the hearing on motion for judgment on the pleadings [55-1], presently scheduled for 10/20/03 shall be continued to 10:00 11/10/03; and any opposition to the Motion for Judgment on the Pleadings shall be served and filed twenty-one (21) days before the hearing date. Reply shall be served and filed seven (7) days before the hearing (el) (Entered: 10/07/2003) |
| 10/16/2003 | 60 | EX PARTE APPLICATION filed by defendant Genentech Inc for case management conference related to NOERR motions Lodged order (el) (Entered: 10/20/2003) |
| 10/16/2003 | 61 | DECLARATION of Daniel M Wall by defendant Genentech Inc of ex parte application for case management conference related to NOERR motions [60-1] (el) (Entered: 10/20/2003) |
| 10/16/2003 | 62 | EX PARTE APPLICATION filed by plaintiff Medimmune Inc for an order consolidating the briefing schedule and hearings on defendnants' [*sic*] motion for judgment on the pleadings and motion for summary judgment . Declaration of Jeffrey R Witham; Lodged Order (el) (Entered: 10/20/2003) |
| 10/16/2003 | 63 | DECLARATION of Jeffrey R Witham in support by plaintiff Medimmune Inc of ex parte application for an order consolidating the briefing schedule and hearings on |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | defendants' motion for judgment on the pleadings and motion for summary judgment [62-1] (el) (Entered: 10/20/2003) |
| 10/17/2003 | 64 | RESPONSE by defendant Celltech R&D Ltd to ex parte application for an order consolidating the briefing and hearings on defendnants' [*sic*] motion for judgment on the pleadings and motion for summary judgment [62-1], and ex parte application by Genentech's case management conference related to NOERR motions [60-1] (el) (Entered: 10/20/2003) |
| 10/17/2003 | 65 | DECLARATION of Charles S Barquist in support by defendant Celltech R&D Ltd of response to ex parte applications by Medimmune Inc for an order consolidating the briefing schedule and hearings on defendants' motion for judgment on the pleadings and for summary judgment [62-1] and Genentech Inc's ex parte application for case management conference related to NOERR motions [60-1] (el) (Entered: 10/20/2003) |
| 10/17/2003 | 66 | MINUTES: (IN CHAMBERS) In chambers and offs [*sic*] the record, a conference call is held. Court and counsel discuss the status of the case, Genentech's Ex Parte for a Case Management Conference is now moot. Court instructs counsel as to Medimmune's Ex Parte Request if in need of further action by the court, they are to contact the Clerk to Judge Pfaelzer by Monday, 10/10/03. Off the record counsel orally stipulate they have |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | come to an agreement as to Medimmune's Ex Parte Request. Medimmune's Ex Parte Request for an order consolidating the briefing schedule and hearings on defendnants' [*sic*] motion for judgment on the pleadings and motion for summary judgment [62-1] is now moot. by Judge Mariana R. Pfaelzer CR: None Present (el) (Entered: 10/21/2003) |
| 10/21/2003 | 67 | MINUTES: (IN CHAMBERS) The parties' request for a stipulated protective order has been referred to the magistrate judge and is DENIED WITHOUT PREJUDICE. The Court declines to sign the overboard protective order (see document for details) by Judge Mariana R. Pfaelzer (el) (Entered: 10/22/2003) |
| 10/23/2003 | 68 | STIPULATION and ORDER by Judge Mariana R. Pfaelzer Defendant Genentech Inc shall file and serve its motion for summary judgment on October 31, 2003. Plaintiff medimmune Inc shall file and serve a combined opposition to GEnentech Inc's motion for summary judgment and Celltech R&D Ltd's motion for judgment on the pleadings on November 17, 2003. Defendant Genentech Inc shall file and serve its reply brief in support of its motion for summary judgment on December 5, 2003. Defendant Celltech R&D Ltd shall file and serve its reply brief in support of its motion for judgment on the pleadings on December 5, 2003. The Court shall hear argument on Genetech Inc's motion for summary judg- |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | ment and Celltech R&D motion for judgment on the pleadings at 10:00am on December 15, 2003. There will be no further continuance of the briefing schedule or the hearing on Celltech R&D Ltd's motion for judgment on the pleadings [55-1] (pj) (Entered: 10/27/2003) |
| 10/31/2003 | 69 | NOTICE OF MOTION AND MOTION by defendant Genentech Inc for summary judgment on plaintiffs antitrust claims ; motion hearing on 12/15/03 at 10:00 a.m.; Memorandum in support; Lodged proposed statement (el) (Entered: 11/03/2003) |
| 10/31/2003 | 70 | MEMORANDUM IN SUPPORT by defendant Genentech Inc of motion for summary judgment on plaintiffs antitrust claims [69-1] (el) (Entered: 11/03/2003) |
| 10/31/2003 | 71 | NOTICE OF APPLICATION AND APPLICATION filed by defendant Genentech Inc for leave to file under seal certain exhibits to declaration of Vernon M Winters ; Memorandum of Points and Authorities in support. Lodged proposed order and exhibit Nos. 13 and 14 (el) (Entered: 11/03/2003) |
| 10/31/2003 | 72 | DECLARATION of Timothy R Schwartz in support by defendant Genentech Inc re application for leave to file under seal certain exhibits to declaration of Vernon M Winters [71-1] (el) (Entered: 11/03/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 10/31/2003 | 73 | DECLARATION of Christopher S Yates in support by defendant Genentech Inc re application for leave to file under seal certain exhibits to declaration of Vernon M Winters [71-1] (el) (Entered: 11/03/2003) |
| 10/31/2003 | 74 | DECLARATION of Sharon E Crane Ph.D. by defendant Genentech Inc re application for leave to file under seal certain exhibits to declaration of Vernon M Winters [71-1] (el) (Entered: 11/03/2003) |
| 10/31/2003 | 75 | DECLARATION of Vernon M Winters by defendant Genentech Inc in support of application for leave to file under seal certain exhibits to declaration of Vernon M Winters [71-1] (el) (Entered: 11/03/2003) |
| | | * * * * |
| 11/04/2003 | 77 | JOINDER by defendant Celltech R&D Ltd joining application for leave to file under seal certain exhibits to of Vernon M Winters [71-1] (el) (Entered: 11/05/2003) |
| 11/07/2003 | 79 | ORDER by Judge Mariana R. Pfaelzer that Genentech's application for leave to file under seal certain exhibits to declaration of Vernon M Winters [71-1] is GRANTED as follows: 1. The non-redacted version of the Declaration of Vernon M Winters that was lodged confidentially under seal with the Court 10/31/03 shall be filed under seal. 2. No persons other than the Court and counsel of record are authorized to inspect the above-listed records (see document for list) filed under seal. (el) (Entered: 11/07/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 11/07/2003 | 80 | JOINT CLAIM CONSTRUCTION STATEMENT by plaintiff and defendants (el) (Entered: 11/10/2003) |
| 11/10/2003 | 85 | ORDER by Judge Mariana R. Pfaelzer that plaintiff Medimmune Inc's application for leave to file under seal its opposition, Statement of Genuine Issues, supporting declaration of aldo Badini and exhibits to Hunter declaration of Tanya Hunter [83-1] is GRANTED. (el) (Entered: 11/21/2003) |
| 11/17/2003 | 81 | MEMORANDUM OF POINTS SNA AUTHORITIES filed by plaintiff Medimmune Inc in opposition to defendant Celltech R&D's motion for judgment on the pleadings [55-1], and defendant Genentech Inc's motion for summary judgment on plaintiffs antitrust claims [69-1] (el) (Entered: 11/18/2003) |
| 11/17/2003 | 82 | STATEMENT OF GENUINE ISSUES OF MATERIAL FACT and reponses to proposed conclusions of law in opposition by plaintiff Medimmune Inc to Genentech Inc's motion for summary judgment on plaintiffs antitrust claims [69-1] (el) (Entered: 11/18/2003) |
| 11/17/2003 | 83 | APPLICATION filed by plaintiff Medimmune Inc for leave to file under seal its opposition, Statement of Genuine Issues, supporting declaration of aldo Badini and exhibits to Hunter declaration Memorandum of Points and Authorities in support; Declaration of Tanya Hunter Lodged Ord (el) (Entered: 11/18/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | * * * * |
| 11/17/2003 | 87 | DECLARATION of Tanya Hunter in support by plaintiff Medimmune Inc of denial or continuance of summary judgment under FRCP 56(F) [69-1] (el) (Entered: 11/24/2003) |
| 11/17/2003 | 88 | DECLARATION of Aldo A Badini in support of plaintiff Medimmune Inc's request for denial or continuance of motion for summary judgment on antitrust claims [69-1] (el) (Entered: 11/24/2003) |
| 11/17/2003 | 89 | DECLARATION of Harvey Kurzweil in support by plaintiff Medimmune Inc's request for denial or continuance of motion for summary judgment on antitrust claims [69-1] (el) (Entered: 11/24/2003) |
| 11/24/2003 | 93 | JOINT NOTICE OF MOTION AND MOTION for protective order ; Declarations of-William Bertrand, John Slater, Timothy Schwartz and Gordon A Goldsmith in support thereof (shb) (Entered: 11/25/2003) |
| 11/24/2003 | 94 | JOINDER by defendant Celltech R&D Ltd joining Medimmune's application for leave to file certain documents under seal; Declaration of John A.D. Slater; Lodged proposed order (shb) (Entered: 11/25/2003) |
| 12/03/2003 | 95 | ORDER by Judge Mariana R. Pfaelzer It is therefor ordered that Medimmune's application for leave to file under sela is GRANTED IN PART. The non-redacated versions of Medimmune's opposition, Statement, Declaration, and Exhibits lodged |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | under seal shall be filed under seal [93-1] (pj) (Entered: 12/05/2003) |
| 12/05/2003 | 96 | APPLICATION filed by defendant Celltech R&D Ltd for leave to file its reply brief under seal ; Lodged order and sealed reply brief (el) (Entered: 12/09/2003) |
| 12/05/2003 | 97 | REPLY BRIEF by defendant Celltech R&D Ltd in support of its motion for judgment on the pleadings [55-1] (el) (Entered: 12/09/2003) |
| | | * * * * |
| 12/05/2003 | 99 | APPLICATION filed by defendant Genentech Inc for leave to file under seal a portion of Genentech Inc's reply memorandum in support of motion for summary judgment on plaintiffs antitrust claims ; Memorandum of Points and Authorities in support; Lodged prop ord prop under seal document (el) (Entered: 12/09/2003) |
| 12/05/2003 | 100 | REPLY MEMORANDUM by defendant Genentech Inc in support of motion for summary judgment on plaintiffs antitrust claims [69-1] (el) (Entered: 12/09/2003) |
| 12/05/2003 | 101 | SUPPLEMENT by defendant Genentech Inc re declaration of CHRISTOPHER S YATES [73-1] (el) (Entered: 12/09/2003) |
| | | * * * * |
| 12/08/2003 | 103 | ORDER by Judge Mariana R. Pfaelzer that Celltech's application for leave to file its reply brief under seal [96-1], is GRANTED. (el) (Entered: 12/17/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 12/08/2003 | 105 | ORDER by Judge Mariana R. Pfaelzer granting application for leave to file under seal a portion of Genentech Inc's reply memorandum in support of motion for summary judgment on plaintiffs antitrust claims [99-1] (el) (Entered: 12/17/2003) |
| 12/08/2003 | 107 | JOINT STIPULATION REGARDING ENTRY OF STIPULATED PROTECTIVE ORDER and ORDER by Judge Mariana R. Pfaelzer that the parties must follow Local Rule 79-5 for making applications to the Court for filing documents under seal. (el) (Entered: 12/17/2003) |
| 12/08/2003 | 108 | STIPULATED PROTECTIVE ORDER by Judge Mariana R. Pfaelzer that this Protective Order shall apply to all information, documents and other items subject to discovery in this action, including without limitation testimony adduce at depositions upon oral examination or upon written questions pursuant to Rules 30 and 31, etc (see document for specifics) (el) (Entered: 12/17/2003) |
| 12/15/2003 | 110 | MINUTES: Counsel present, hearing held. Oral argument heard, Court takes the motion for judgment on the pleadings [55-1] and motion for summary judgment on plaintiffs antitrust claims [69-1], under submission and will issue an order at a later date submitted by Judge Mariana R. Pfaelzer CR: Margaret Babykin (el) (Entered: 12/24/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 12/22/2003 | 109 | JOINDER by defendant City of Hope Nati joining opening brief regarding claim construction. (bp) (Entered: 12/23/2003) |
| 12/22/2003 | 113 | OPENING BRIEF REGARDING CLAIM CONSTRUCTION FILED by defendant Genentech Inc (el) (Entered: 12/24/2003) |
| 12/22/2003 | 114 | DECLARATION of Dean G Dunlavey in support by defendant Genentech Inc's opening brief [113-1] (el) (Entered: 12/24/2003) |
| 12/23/2003 | 111 | MEMORANDUM OF DECISION AND ORDER by Judge Mariana R. Pfaelzer that summary judgment on plaintiffs antitrust claims [69-1], and related state causes of action is GRANTED in favor of the Defendants with respect to the fifth, sixth, eighth, ninth and tenth causes of action in the First Amended Complaint [55-1]. (see document for specifics) (el) (Entered: 12/24/2003) |
| 12/23/2003 | 112 | NOTICE OF DISCREPANCY AND ORDER by Judge Mariana R. Pfaelzer ordering Opening brief, Declaration in support submitted by defendant Genentech Inc received on 12/22/03 to be fld and processed; fld date to be the date the doc was stamped "received but not fld" w/the Clerk (el) (Entered: 12/24/2003) |
| 12/29/2003 | 115 | EX PARTE APPLICATION filed by plaintiff Medimmune Inc for an order extending deadline to file a motion to amend the pleadings Lodged Prop ord (el) (Entered: 12/30/2003) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 12/29/2003 | 116 | DECLARATION of Jeffrey R Witham in support by plaintiff Medimmune Inc re ex parte application extending deadline file a motion to amend the pleadings [115-1] and re notice to other parties (el) (Entered: 12/30/2003) |
| 12/30/2003 | 117 | MINUTES: (IN CHAMBERS) the Court is in receipt of Plaintiffs ex parte application extending deadline to file a motion to amend the pleadings [115-1]. The Court now extends the deadline to file a motion to amend the pleadings from 12/29/03 to 1/12/04. No further continuances will be granted by Judge Mariana R. Pfaelzer CR: None Present (el) (Entered: 2/31/2003) |
| 12/30/2003 | 118 | OPPOSITION by defendant Genentech Inc t [*sic*] Medimmune'so [*sic*] ex parte application for an order extending the deadline to file a motion to amend the pleadings [115-1] (jp) (Entered: 12/31/2003) |
| 12/30/2003 | 119 | OPPOSITION by defendant Celltech R&D Ltd to Medimmune's ex parte application for an order extending the deadline to file a motion to amend the pleadings [115-1] (jp) (Entered: 12/31/2003) |
| 01/14/2004 | 120 | AMENDED MEMORANDUM OF DECISION and Order by Judge Mariana R. Pfaelzer regarding Defendant Genentech's Motion for Summary Judgment[69], and Defendant Celltech's Motion for Judgment on the Pleadings[55]. Based upon the fact that Noerr-Pennington immunity bars Med- |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | Immune's failure to adequately plead any antitrust violation (such as price-fixing in the ARLA) that is not barred by Noerr-Pennington, summary judgment for the Defendants is hereby GRANTED with respect to the fifth, sixth, seventh, eighth, ninth, and tenth causes of action in the First Amended Complaint (see document for details) (el, ) (Entered: 01/15/2004) |
| 01/16/2004 | 123 | OPPOSITION filed by Defendant Genentech Inc to Medimmune's MOTION for Leave to File a Second Amended Complaint [121] (el, ) (Entered: 01/22/2004) |
| 01/16/2004 | 124 | OPPOSITION filed by Defendant Celltech R&D Ltd to Medimmune's MOTION for Leave to File Second Amended Complaint [121] . (el, ) (Entered: 01/22/2004) |
| 01/16/2004 | 125 | DECLARATION of Steven M Haines in opposition to MOTION for Leave to File a Second Amended Complaint [121] filed by Defendant Celltech R&D Ltd. (el,) (Entered: 01/22/2004) |
| | | * * * * |
| 01/20/2004 | 127 | NOTICE OF MOTION AND MOTION for Entry of Final Judgment filed by Defendant Celltech R&D Ltd. Motion set for hearing on 2/9/2004 at 10:00 AM before Honorable Mariana R. Pfaelzer. (el,) (Entered: 01/22/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 01/20/2004 | 128 | NOTICE OF MOTION re MOTION for Entry of Final Judgment[127] filed by Defendant Celltech R&D Ltd. (el,) (Entered: 01/22/2004) |
| | | * * * * |
| 01/21/2004 | 129 | MINUTES In Chambers Conference held before Judge Mariana R. Pfaelzer : The Court, on its own Motion, continues MOTION for Leave to File Second Amended Complaint [121] and Markman Hearing regarding Claim Construction continued to 2/23/2004 at 10:00 AM before Honorable Mariana R. Pfaelzer. Court Reporter: Not Present. (el,) (Entered: 01/22/2004) |
| 01/22/2004 | 139 | JOINT STIPULATION Regarding MOTION to Compel Defendant Genentech Inc.'s Responses to First Set of Request for Production of Documents and Interrogatories[ 138] filed by plaintiff Medimmune Inc. (yl, ) (Entered: 02/05/2004) |
| 01/26/2004 | 134 | OPPOSITION BRIEF regarding Claim Construction filed by Plaintiff Medimmune Inc. (el, ) (Entered: 01/29/2004) |
| 01/26/2004 | 135 | DECLARATION of Jeffrey R Witham in support of Plaintiff Medimmune Inc's Opposition Brief in support of claim construction [134] filed by Plaintiff Medimmune Inc. (el, ) (Entered: 01/29/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 01/27/2004 | 131 | NOTICE OF DISCREPANCY AND ORDER: by Judge Carolyn Turchin, This motion should be filed before Judge Pfaelzer. According to the Judges' Procedures and Schedules on the Court's website, discovery motions are to be scheduled before the District Judge and may, but not necessarily, be referred to the magistrate judge on a motion by motion basis. (dam) (Entered: 01/28/2004) |
| 01/28/2004 | 132 | STIPULATION AND ORDER by Judge Mariana R. Pfaelzer : That 1. The hearing on Celltech's MOTION for Entry of Final Judgment[127] shall be continued for hearing on 2/23/2004 at 10:00 AM before Honorable Mariana R Pfaelzer. 2. Opposition or other response shall be filed and served on or before 2/6/04; 3. Any reply in support of Celltech's motion shall be filed and served by Celltech on or before 2/13/04; 4. Any reply in support of MedImmune's Motion for leave to file a second amended complaint shall be served and filed by MediMMune on or before 2/13/04; and 5. Any reply to Medimmune's opposition brief in support of Claim Construction shall be served and filed by Genentech and/or City of Hope on or before 2/13/04.(el, ) Modified on 1/30/2004 (el, ). (Entered: 01/29/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 01/28/2004 | 133 | ORDER by Judge Mariana R. Pfaelzer regarding Terms to be construed at Markman hearing. That the parties are instructed to meet and confer to reduce the number of Markman claims. No later than Monday, 2/9/04, the parties will file a joint submission of the terms to be decided in the 2/23/04 Markman hearing. The parties will submit this joint statement no later than 2/9/04. Nothing in this Ordershould be construed to otherwise alter the briefing schedule for claim construction.(el, ) (Entered: 01/29/2004) |
| 01/28/2004 | 138 | NOTICE OF MOTION AND MOTION to Compel Defendant Genentech Inc.s Responses to First Set of Requests for Production of Documents and First Set of Interrogatories filed by Plaintiff Medimmune Inc. Motion set for hearing on 2/23/2004 at 10:00 AM before Honorable Mariana R. Pfaelzer. (yi,) (Entered: 02/05/2004) |
| 02/02/2004 | 137 | STIPULATION AND ORDER by Judge Mariana R. Pfaelzer : re Page limits for Claim Construction Briefs per Order, 133; that Defendant Genentech, Inc shall file and serve its opening brief concerning claim construction on 12/22/03. Genentechs brief shall not exceed 45 pages; Plaintiff MedImmune Inc shall file and serve its opposition brief on 1/16/04. Medimmunes opposition brief shall not exceed 45 pages: Defendant Genentech Inc shall file and |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | serve its reply brief concerning claim construction on 1/27/04.(el,) (Entered: 02/04/2004) |
| 02/06/2004 | 140 | NOTICE OF MOTION AND MOTION for Joinder in [127] MOTION for Entry of Judgment filed by Defendant Genentech Inc. Motion set for hearing on 2/23/2004 at 10:00 AM before Honorable Mariana R. Pfaelzer. (el, ) (Entered: 02/11/2004) |
| 02/06/2004 | 141 | STATEMENT filed by Plaintiff Medimmune Inc in response to Defendant Celltech R and D Ltds MOTION for Entry of Final Judgment [127]. (el,) (Entered: 02/11/2004) |
| 02/09/2004 | 142 | SUPPLEMENTAL MEMORANDUM OF LAW in Support of its MOTION to Compel Defendants [138] Genentechs responses to first set of requests for production of documents and interrogatories filed by Plaintiff Medimmune Inc. (el, ) (Entered: 02/13/2004) |
| 02/09/2004 | 143 | JOINT STATEMENT responsive to Courts 1/28/04 Order filed by Defendants Celltech R&D Ltd, City of Hope National Medical Center, Genentech Inc, Plaintiff Medimmune Inc re: Order on terms to be construed at Markman Hearing 133. (el,) (Entered: 02/13/2004) |
| 02/09/2004 | 144 | SUPPLEMENTAL MEMORANDUM IN RESPONSE filed by Defendant Genentech Inc to MOTION to Compel[138] (el,) (Entered: 02/13/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 02/13/2004 | 146 | REPLY BRIEF FILED by Defendant Genentech Inc regarding Claim Construction Brief [113]. (el, ) (Entered: 02/19/2004) |
| 02/13/2004 | 147 | SUPPLEMENTAL DECLARATION of Dean G Dunlavey in support of Defendant Genentech Incs Reply Brief regarding Claim Construction [146] filed by Defendant Genentech Inc. (el,) (Entered: 02/19/2004) |
| 02/13/2004 | 149 | REPLY BRIEF in support of its MOTION for Entry of Final Judgment [127] filed by Defendant Celltech R&D Ltd. (el,) (Entered: 02/20/2004) |
| 02/13/2004 | 152 | JOINDER filed by Defendant City of Hope National Medical Center joining in Brief regarding Claim Construction [146]. (el,) (Entered: 03/03/2004) |
| 02/18/2004 | 145 | MEMORANDUM OF DECISION and ORDER by Judge Mariana R. Pfaelzer : On 1/20/03, Defendant Celltech R&D ("Celltech") filed a Motion for Entry of Final Judgment [127] and [140] Motion for Joinder on said motion. Having determined that oral argument will not assist the Court in considering this motion, this Court hereby vacates the hearing scheduled for 2/23/04, and GRANTS Celltechs motion. This Court enters final judgment on the fifth, sixth, seventh, eighth, ninth and tenth causes of action. Medimmune may pursue the remaining claims, but Celltech will no longer be involved as a party. (el,) (Entered: 02/19/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 02/18/2004 | 148 | MEMORANDUM OF DECISION by Judge Mariana R. Pfaelzer regarding Motion to file Second Amended Complaint. That based on this Court's prior summary judgment decision, and in light of the fact that MedImmune's proposed amendments were unduly delayed and would be futile if allowed, MedImmunes [121], Motion for Leave to File Second Amended Complaint is DENIED in its entirety.(el,) (Entered: 02/19/2004) |
| 02/19/2004 | 150 | MINUTES held before Judge Mariana R. Pfaelzer : The Court, on its own Motion, continues Plaintiffs Motion to Compel Genentech responses to 1st set of interrogatories [138], and Markman hearing re: claim construction to 3/15/2004 at 10:00 AM before Honorable Mariana R. Pfaelzer. Court Reporter: Not Present. (el, ) (Entered: 02/23/2004) |
| 03/04/2004 | 158 | NOTICE OF APPLICATION to Clerk to Tax Costs on Plaintiff Medimmune Inc filed by Defendant Celltech R&D Ltd. Lodged Bill of Cost. (el, ) (Entered: 03/24/2004) |
| 03/08/2004 | 153 | JOINT APPLICATION Requesting a telephonic status conference to discuss subject matter jurisdiction and scheduling in light of the 3/5/04 decision of the Federal Circuit in Gen-Probe Inc v Vysis Inc filed by Defendant Genentech Inc. Lodged proposed order. (el, ) (Entered: 03/11/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 03/10/2004 | 154 | MINUTES In Chambers Conference held before Judge Mariana R. Pfaelzer : Held Conference call. Parties discuss rulings in Gen-Probe v. Vysis, The Markman hearing will not be held until the motion to dismiss is resolved. The Court stays the action. Case stayed. Counsel will submit a stipulation and proposed order. Court Reporter: Mark Schweitzer. (el, ) (Entered: 03/11/2004) |
| 03/11/2004 | 159 | OPPOSITION to Celltech R&D's APPLICATION to Tax Costs [158] filed by Plaintiff Medimmune Inc. (el, ) (Entered: 03/24/2004) |
| 03/11/2004 | 160 | OPPOSITION to Celltech R&D's APPLICATION to Tax Costs [158] filed by Plaintiff Medimmune Inc. (el,) (Entered: 03/24/2004) |
| 03/12/2004 | 155 | JUDGMENT by Judge Mariana R. Pfaelzer, This Court enters FINAL JUDGMENT on the fifth, sixth, seventh, eighth, ninth and tenth causes of action. This Order is final judgment for purposes. It shall be entered pursuant to FRCP 58 AND 79(a) and served upon the parties(pj, ) (Entered: 03/15/2004) |
| 03/12/2004 | 156 | STIPULATION AND ORDER the hearing on Defendants motion to dismiss remaining causes of action for lack of subject matter jurisdiction will be held on Monday, April 19, 2004 10:00am. Genentech and/or City of Hope will file Opening brief March 22, 2004, Medimmune will file Opposition brief no later than March 29, 2004. Genetech |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | and/or City of Hope Reply Briefs April 4, 2004. All other proceedings and discovery in this matter are stayed pending resolution of the motion to dismiss by Judge Mariana R. Pfaelzer :(pj, ) (Entered: 03/15/2004) |
| 03/15/2004 | 161 | RESPONSE filed by defendant Celltech to Medimmune Ines Opposition to APPLICATION to Clerk to Tax Costs[158] . (el, ) (Entered: 03/24/2004) |
| 03/15/2004 | 162 | DECLARATION of Jason A Crotty regarding Celltechs APPLICATION to Tax Costs [158] filed by Defendant Celltech R&D Ltd. (el, ) (Entered: 03/24/2004) |
| 03/17/2004 | 157 | NOTICE OF APPEAL to Federal Circuit Court filed by plaintiff Medimmune Inc. Appeal of Judgment, 155 Filed On: 3/12/04; Entered On: 3/15/04; Filing fee $255, Paid receipt number 13647. cc: Jeffrey R. Witham; Dewey Ballantine; Carella, Byrne, Bain, Gilfillan, Cecchi, Stewart and Olstein; Latham and Watkins, San Francisco; Latham and Watkins, Los Angeles: Latham and Watkins, Costa Mesa; Keker and Van Nest; Ira and Manella: Morrison and Foerster, Los Angeles; Morrison & Foerster, San Francisco. (weap, ) (Entered: 03/17/2004) |
| 03/18/2004 | 163 | BILL OF COSTS. Costs Taxed in amount of $ $6,150.45 in favor of Celltech R and D Ltd and against Medimmune Inc. RE: Judgment, 155 (el, ) (Entered: 03/24/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 03/18/2004 | | BILL OF COSTS. Costs Taxed in amount of $ $6,150.45 in favor of Celltech and against Medimmune Inc. RE: Judgment, 155 (el, ) (Entered: 03/24/2004) |
| 03/22/2004 | 164 | NOTICE OF MOTION AND MOTION to Dismiss for Lack of Jurisdiction filed by Defendant Genentech Inc. Motion set for hearing on 4/19/2004 at 10:00 AM before Honorable Mariana R. Pfaelzer; Memorandum of Points and Authorities in support. (el, ) (Entered: 03/26/2004) |
| 03/23/2004 | 166 | NOTICE OF MOTION AND MOTION for Joinder in [164] MOTION to Dismiss for Lack of Jurisdiction filed by Defendant City of Hope National Medical Center. (yl,) (Entered: 04/08/2004) |
| 03/29/2004 | | Transmission of Notice of Appeal and Docket Sheet to US Court of Appeals re: Appeal to Circuit Court [157]. (ghap,) (Entered: 03/29/2004) |
| 03/29/2004 | 167 | PROOF OF SERVICE filed by Plaintiff Medimmune Inc. Plaintiffs Opposition to Genetech Inc's Motion to Dismiss for Lack of Subject Matter Jurisdiction, etc (see document was further details) was served on 3/29/04. (yi, ) (Entered: 04/08/2004) |
| 03/29/2004 | 170 | DECLARATION of Tanya Hunter in Support of Plaintiffs Opposition to Motion to Dismiss for Lack of Jurisdiction[164] filed by Plaintiff Medimmune Inc. (yl, ) (Entered: 04/08/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 03/29/2004 | 171 | OPPOSITION TO GENETECH [*sic*] INC'S MOTION to Dismiss for Lack of Jurisdiction[164] filed by Plaintiff Medimmune Inc. (yl,) (Entered: 04/08/2004) |
| 04/02/2004 | 165 | NOTICE to Prepare Reporter's Transcript filed by plaintiff Medimmune Inc. (wdc, ) (Entered: 04/05/2004) |
| 04/05/2004 | 172 | REPLY BRIEF IN SUPPORT Of MOTION to Dismiss for Lack of Jurisdiction[164] filed by Defendant City of Hope National Medical Center. (yl, ) (Entered: 04/09/2004) |
| 04/05/2004 | 174 | REPLY BRIEF in support of MOTION to Dismiss for Lack of Jurisdiction [164] filed by Defendant Genentech Inc. (shb,) (Entered: 04/12/2004) |
| 04/05/2004 | 175 | REQUEST FOR JUDICIAL NOTICE in support of MOTION to Dismiss for Lack of Jurisdiction [164] filed by Defendant Genentech Inc. Request set for hearing on 4/19/2004 at 10:00 AM before Honorable Mariana R. Pfaelzer. (shb,) (Entered: 04/12/2004) |
| | | * * * * |
| 04/13/2004 | 176 | NOTIFICATION by Circuit Court of Appellate Docket Number 04-1300, Federal Circuit Court regarding Appeal to Circuit Court, [157] filed by Medimmune Inc. (cbr, ) (Entered: 04/15/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 04/19/2004 | 177 | PROCEEDINGS: held before Judge Mariana R. Pfaelzer : 1. Genentechs Motion to dismiss for lack of subject matter jurisdiction. 2. Joinder by defendant City of Hope. 3. Request for judicial notice in support of Motion to dismiss. Hears argument. The court takes the matter under submission and will issue the order. Court Reporter: Gail Peoples. (el, ) (Entered: 04/20/2004) |
| | | * * * * |
| 04/22/2004 | 179 | MEMORANDUM OF DECISION AND ORDER by Judge Mariana R. Pfaelzer re MOTION to Dismiss for Lack of Jurisdiction[164]. Because the Gen-Probe decision dictates that this Court does not have subject matter jurisdiction over Medimmunes suit for declaratory judgment, Genetechs Motion is GRANTED and the First, Second, Third and Fourth Causes of Actions are dismissed as to both Genetech and City of Hope. (Made JS-6. Case Terminated)(el, ) (Entered: 04/23/2004) |
| 04/26/2004 | 180 | AMENDED MEMORANDUM OF DECISION AND ORDER by Judge Mariana R. Pfaelzer re MOTION to Dismiss for Lack of Jurisdiction [164]. Having considered the parties written and oral argument this court GRANTS the Defendants motion. Because the Gen-Probe decision dictates that this Court does not have subject matter jurisdiction over MedImmunes suit for declaratory judgment, Genentechs Motion is GRANTED and the First, Second, Third and |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | Fourth Causes of Actions are dismissed as to both Genetech and City of Hope. (see document for specifics)(el,) (Entered: 04/27/2004) |
| 04/28/2004 | 181 | REQUEST for Entry of Judgment filed by Plaintiff Medimmune Inc. Lodged proposed order. (el, ) (Entered: 04/30/2004) |
| 04/29/2004 | 182 | STATEMENT OF NO OPPOSITION re Medimmunes REQUEST for Entry of Judgment [181] filed by Defendant Genentech Inc. (el, ) (Entered: 04/30/2004) |
| 04/30/2004 | 183 | ENTRY OF JUDGMENT by Judge Mariana R. Pfaelzer: this Court enters final judgment on the first, second, third and fourth causes of action and hereby dismisses those claims as to both Genentech, Inc. and City of Hope. All claims and all defendants are hereby dismissed. This Order is a final judgment for purposes of Fed.R.Civ.P.54(a). It shall be entered pursuant to Fed. R.Civ.P.58 and 79(a), and served upon the parties.(pbap, ) Modified on 5/3/2004 (pbap, ). (Entered: 05/03/2004) |
| 04/30/2004 | 185 | STATEMENT of NON OPPOSITION to REQUEST for entry of Judgment[181] filed by defendant City of Hope National Medical Center. (lc, ) (Entered: 05/07/2004) |
| 04/30/2004 | 187 | NOTICE OF ERRATA filed by Plaintiff Medimmune Inc correcting Response in Opposition to Motion to dismiss for lack of subject matter jurisdiction [171] (el,) (Entered: 05/12/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 05/05/2004 | 184 | NOTICE OF APPEAL to Federal Circuit Court filed by plaintiff Medimmune Inc. Appeal of Judgment, 183 Filed On: 4/30/04; Entered On: 5/3/04; Filing fee $255., Paid receipt number 64898. cc: Jeffrey R. Witham; Dewey Ballantine; Elliot M. Olstein; Latham and Watkins, San Francisco; Latham and Watkins, Los Angeles; Latham and Watkins, Costa Mesa; Keker and Van; Irell and Manella; Morrison and Foerster, Los Angeles; Morrison and Foerster, San Francisco. (weap, ) (Entered: 05/05/2004) |
| 05/05/2004 | 189 | APPLICATION to Clerk to Tax Costs on Medimmune Inc Re: Amended Memorandum & Opinion 180; Memorandum & Opinion, 179 filed by Defendant City of Hope National Medical Center. (el, ) (Entered: 05/28/2004) |
| | | * * * * |
| 05/12/2004 | | Transmission of Notice of Appeal and Docket Sheet to US Court of Appeals re: Appeal to Circuit Court, [184]. (ghap, ) (Entered: 05/12/2004) |
| 05/12/2004 | 190 | STATEMENT of Non-Opposition to Defendants APPLICATION to Tax Costs re Medimmune Inc [189] filed by Plaintiff Medimmune Inc. (el, ) (Entered: 05/28/2004) |
| 05/18/2004 | 195 | NOTICE OF APPLICATION TO CLERK TO TAX COSTS filed by Defendant Genentech Inc. (pj, ) (Entered: 06/09/2004) |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| 05/20/2004 | 191 | BILL OF COSTS. Costs Taxed in amount of $ $2,209.41 in favor of City of Hope and against MedImmune Inc. RE: Judgment, 183 (el, ) (Entered: 05/28/2004) |
| 05/20/2004 | 192 | BILL OF COSTS. Costs Taxed in amount of $ $2,209.41 in favor of City of Hope and against MedImmune Inc. RE: Judgment, 183 (el, ) (Entered: 05/28/2004) |
| 05/26/2004 | 193 | NOTIFICATION by Circuit Court of Appellate Docket Number Federal Circuit Cour, 04-1384 regarding, Appeal to Circuit Court, [184] filed by Medimmune (cbr, ) (Entered: 05/28/2004) |
| 05/27/2004 | 196 | OPPOSITION to application to clerk to tax costs[195] filed by Plaintiff Medimmune Inc. (pj, ) (Entered: 06/09/2004) |
| 05/28/2004 | 194 | NOTICE OF CLERICAL ERROR Re: Costs Taxed[191] should not have a document number since the same document gets a number under the Bill of Costs event, which in this case is #192. (el, ) (Entered: 05/28/2004) |
| 05/28/2004 | 197 | RESPONSE filed by Defendant Genentech Inc to opposition [196] (pj, ) (Entered: 06/09/2004) |
| 06/03/2004 | 198 | BILL OF COSTS. Costs Taxed in amount of $ 10,322.56 in favor of Genentech Inc and against Medimmune. RE: Judgment, 183. Counsel stipulate to $10,322.56 with teh [*sic*] understanding that neither side to retax (pj,) (Entered: 06/09/2004) |

| DATE | NO. | PROCEEDINGS |
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| | | * * * * |
| 03/02/2005 | 200 | RECORD ON APPEAL sent to Federal Circuit Court re: Appeal number, 04-1300 Record consists of 1 through 10 volumes, 5 transcripts; 5 brown folders # B0058, B0075, B0089, B0114, B0170; 14 sealed documents # 86, 90, 91, 92, 93, 104, 106, 121, 122, 136, 151, 168, 169, 188. (ghap, ) Modified on 3/2/2005 (ghap, ). Modified on 3/2/2005 (fvap, ). (Entered: 03/02/2005) |
| 10/18/2005 | 201 | ORDER from Federal Circuit filed as to Appeal to Circuit Court, [157] filed by Medimmune Inc, Appeal Number Info from USCA (A-8)[176], CCA # 04-1300. Order received in this district on 10/24/05. Notice of entry of judgment accompanied by opinion. (ghap, ) Modified on 10/28/2005 (ghap, ). (Entered: 10/28/2005) |
| 11/08/2005 | 202 | MANDATE of 9th CCA filed as to Appeal to Circuit Court [157], Appeal Number Info from USCA (A-8)[176], Appeal to Circuit Court [184], Appeal Number Info from USCA (A-8)[193], CCA # 04-1300 and 04-1384. The appeal is AFFIRMED. Mandate received in this district on 11/17/2005. (jp, ) (Entered: 11/22/2005) |
| 12/13/2005 | 203 | Appeal Record Returned from 9th CCA RE: RECORD ON APPEAL sent to Federal Circuit Court re: Appeal number, 04-1300 Record consists of 1 through 10 volumes, 5 transcripts; 5 brown folders # B0058, B0075, B0089, B0114, B0170; 14 sealed documents # 86, 90, 91, 92, 93, 104, 106, |

| DATE | NO. | PROCEEDINGS |
|---|---|---|
| | | 121, 122, 136, 151, 168, 169, 188. (ghap, ) Modified on 3/2/2005 (ghap, ). Modified on 3/2/2005 (fvap, ). Received: Volume(s): 1 through 10; Transcripts(s): 5; brown folders # 58, 75, 89, 114, 170;14 sealed. (ghap, ) (Entered: 12/15/2005) |

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

No. 04-1300

DOCKET ENTRIES

MEDIMMUNE

v.

GENENTECH

CONSOLIDATED W/APPEAL(S) 04-1384.
CONSOLIDATED APPEAL(S) DOCKETED: 05/20/04

U.S. District Court
Central District of California

Lower Court/Agency #: 03-CV-2567
Notice of Appeal and Certified List Received: 04/06/04
Notice of Appeal Filed: 03/17/04

* * * *

PROCEEDINGS*

1. Certificate of Interest for Defendant Appellee(s), City of Hope, filed (04/20/04) not served. Received: 04/20/04 (EOD 04/27/04) (SKS) 04-1300

2. Certificate of Interest for Appellee(s), Genentech, Inc. Filed (05/03/04) MS 4/30/04. Received: 05/03/04 (EOD 05/05/04) (SKS) 04-1300

3. Certificate of Interest for Appellant(s), Medimmune, Inc. Filed (04/27/04) MS 4/20/04. Received: 04-27-04 (EOD 05/05/04) (SKS) 04-1300

* Capitals in original entries deleted.

PROCEEDINGS

4. Note to File: Lead Appeal 04-1300 is consolidated with appeal 04-1384 (filed by Medimmune on 5/5/04), Docketed 5/20/04. Filed 05/20/04 (EOD 05/20/04 (AMT) 04-1300

5. Official caption revised. (MS-05/20/04) Filed: 05/20/04 (EOD 05/20/04 (AMT) 04-1300

6. Certificate of compliance pursuant to rule 11(d), received from appellant. (MS-05/21/04) Filed: 05/24/04 (EOD 05-25-04) (LP) 04-1300

7. Certificate of compliance pursuant to rule 11(d), received from appellee(s), Filed (05/25/04) (MS-05/24/04) Received: 05-25-04 (EOD 05/27/04) (SKS) 04-1300

8. Recd Appellee Genentech's certificate of compliance with Federal Circuit Rule 11(d). (MS-05/23/04) Received: 05/24/04 (EOD 05/27/04) (KSH) 04-1300

9. Recd Appellee Celltech R&D LTD. certificate of compliance with rule 11(b). (MS-05/24/04) Received: 05/25/04 (EOD 05/27/04) (KSH) 04-1300

10. Appellant - Unopposed motion for extension of time to file appellant's initial brief. (MS-05/27/04) Filed: 05/28/04 On consent. Action on Motion (11): Granted. Brief is due July 7, 2004. By clerk. Filed: 06/02/04. (EOD 06/02/04 by CLT) The brief is due on 07/07/04. 04-1300

12. Appellee's LTR apprising court of an error made in a revised official caption. (Noted and corrected revised official caption was sent to parties). (MS-06/02/04) Received: 05/27/04 (EOD 06/03/04) (LP) 04-1300

Medimmune, Inc. (Appellant) - Brief of plaintiff-appellant Medimmune, Inc. (MS-07/07/04). Filed: 07/07/04 [042555] (EOD 07/09/04 by VW_) 04-1300

PROCEEDINGS

13. Certificate of compliance with Federal Circit Rule 11(d) by the Plaintiff-Appellant, Medimmune, Inc. (MS-07/02/04) Received: 07/02/04 (EOD 07/19/04) (CTD) 04-1300

14. Appellee - Unopposed motion for City of Hope and Genetech, Inc for an extention of time to file the appellee's brief. (MS-07-27-04) Received: 07/27/04. On consent. Action on motion (15): Granted. By clerk. Brief is due September 15, 2004. By clerk. Filed: 07/28/04 (EOD 07/28/04 by CTD) The brief is due on 09/15/04. 04-1300

16. Appellant - Unopposed motion of Medimmune, Inc. for extention of time to file Appellant's Reply Brief. (MS-08/10/04) Filed: 08/11/04 On consent. Action on motion (17): Motion granted. The brief is due on 10/15/04. By clerk. Filed: 08/12/04 (EOD 08/13/04 by JB) 04-1300

City of Hope [appellee] - Brief of Defendant-Appellee City of Hope (MS-09/14/04). Received: 09/15/04. Rejected: 09/20/04. Corrected Brief due: 10/04/04. [042615] (EOD 09/20/04 by LS_) 04-1300

Celltech R&D, LTD. [appellee] - Brief for Defendant-Appellee Celltech R&D LTD. (MS-09/15/04). Received: 03/16/04. Rejected: 09/20/04. Corrected Brief due: 10/04/04. [042615] (EOD 09/20/04 by LS_) 04-1300

Genentech, Inc. [appellee] Brief of Defendant-Appellee Genentech, Inc. (MS-09/15/04). Received: 09/15/04. Rejected: 09/20/04. Corrected Brief due: 10/04/04. [042615] (EOD: 09/20/04 by LS_) 04-1300

18. Amended certificate of interest for the defendant-appellee, City of Hope. (MS-09/15/04) Received: 09/15/04 (EOD 09/21/04) (CTD) 04-1300

Celltech R&D, LTD. [Appellee] - corrected brief for defendant-appellee Celltech R&D LTD. (MS-09/27/04). Corrected brief received: 09/27/04. Filed: 09/15/04 [042615] (EOD 09/29/04 by LS_) 04-1300

Genentech, Inc. [appellee] - corrected brief of Defendant-Appellee Genentech, Inc. (MS-09/24/04). Corrected brief received: 09/24/04. Filed: 09/15/04. [042615] (EOD 09/29/04 by LS_) 04-1300

City of Hope [appellee] - corrected brief of Defendant-Appellee City of Hope (MS-09/24/04). Corrected brief received: 09/27/04. Filed: 09/14/04. [042615] (EOD 09/29/04 by LS_) 04-1300

19. Appellee's LTR confirming telephone call regarding deadline for filing initial brief. (Noted) (MS-09/23/04) Received: 09/28/04) (EOD 09/30/04) (LP) 04-1300

20. Appellant - Motion to request judicial notice of court records. [NPF] (MS-10/15/04). Filed: 10/15/04 Action on motion (23): Motion granted. By motions panel. Judge: Gajarsa. Filed: 11/24/04. (EOD 11/24/04 by ETW) 04-1300

Medimmune, Inc. [appellant] - Reply brief of Plaintiff-Appellant Medimmune, Inc. (MS-10/15/04). Filed: 10/15/04. [052642] (EOD 10/18/04 by VW_) 04-1300

Medimmune, Inc. [appellant] - Joint appendix (Volumes I-III) (MS-10/25/04). Filed: 10/25/04. [confidential & nonconfidential versions] Entry of appearance notice issued. [052653] (EOD 11/01/04 by LS_) 04-1300

21. Joint statement of compliance with rule 33. (MS-10/26/04) Received: 10/26/04 (EOD 11/02/04) (CTD) 04-1300

22. Amended certificate of interest on behalf of Plaintiff-Appellant, Medimmune, Inc. (HS-11/12/04) Received: 11/12/04 (EOD 11/16/04) (SB) 04-1300

    December 22, 2004 Notice of calendaring issued. Panel 0502E on February 10, 2005 04-1300 (KSH)

24. Recd Appellant's citation of supplemental authority. (Sent to Panel) (HS-01/14/05) Received: 01/14/05 (EOD 01/14/05) (KSH) 04-1300

    February 10, 2005 Submitted after Oral Argument by Harvey Kurzwell and D. Wall, C. Barquist. 04-1300 (KSH) (Newman, Mayer and Clevenger)

25. Record requested from DCT-CD/CA on 02/16/05. Due: 03/04/05. [30] Returned: 11/17/05. Rev (11/17/05 by CLT) 2004-1300

26. Affirmed. Precedential opinion by Newman, J. Judgment entered on 10/18/05. Separate opinion dissenting in part by Clevenger, J. Entered by clerk. (MS-10/18/05) Received: 10/18/05 (EOD 10/18/05) (KSH) 04-1300

27. Appellee's (Celltech) stipulated bill of costs against Appellant, Received. (MS-10/31/05) Filed: 11/01/05 30. Allowable costs: $400.00 11/08/05 (EOD 11/08/05) (CLT) 04-1300

28. Appellee's (City of Hope) stipulated bill of costs against Appellant, Received. (MS-11/01/05) Filed: 11/02/05 31. Allowable costs: $200.00 11/08.05 (EOD 11/08/05 (CLT) 04-1300

29. Appellee's (Genentech, Inc.) stipulated Bill of Costs against Appellant, Received. (MS-11/01/05) Filed: 11/01/05 32. Allowable costs: $750.00 11/08/05 (EOD 11/08/05) (CLT) 04-1300

    Mandate issued to the DCT: 11/08/05. (EOD 11/08/05 by CLT) 04-1300

PROCEEDINGS

33. Petition for writ of certiorari filed 10/18/05. Supreme Court #:05-608. (EOD 11/30/05 by AV) 04/1300. (See entry #35)

Docket entries made after this point were made in the new case management system.

35. Petition for Writ of Certiorari filed 10/18/05. Supreme Court #05-608. Cert. Granted on 02/21/06. REV (02/21/06 by AVV) 2004-1300

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

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Case No. CV 03-2567

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MEDIMMUNE, INC.,

*Plaintiff*,

v.

GENENTECH, INC., CITY OF HOPE NATIONAL MEDICAL CENTER, and CELLTECH R&D LTD.

*Defendants*.

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PLAINTIFF MEDIMMUNE, INC.'S COMPLAINT FOR:

1. Declaratory Judgment;
2. Patent Invalidity;
3. Patent Unenforceability;
4. Non-Infringement;
5. Section 1 of the Sherman Act;
6. Section 2 of the Sherman Act;
7. The Cartwright Act;
8. Section 17200 of the Cal. Bus. & Profs. Code; and
9. Unjust Enrichment.

DEMAND FOR JURY TRIAL

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*JURISDICTION AND VENUE*

1. Plaintiff MedImmune, Inc. ("MedImmune") seeks declaratory relief pursuant to Fed. R. Civ. P. 57 and 28 U.S.C. §§ 2201 and 2202. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331, 1337 and 1338(a). This Court has jurisdiction over the state law claims asserted hereunder pursuant to 28 U.S.C. § 1367. This Court has personal jurisdiction over defendant Genentech, Inc. ("Genentech") based

on its principal place of business in California. This Court has personal jurisdiction over defendant City of Hope National Medical Center ("CHNMC") based on its organization under the laws of the state of California and because its principal place of operation is in California. This Court has personal jurisdiction over defendant Celltech R&D Ltd. ("Celltech") based on its activities in this jurisdiction, including, but not limited to, Celltech's filing of a suit against Genentech under 35 U.S.C. § 146 in the Northern District of California captioned *Celltech R&D Ltd. v. Genentech, Inc.*, Civ. Act 01-3560JCS (N.D. Cal. 2001).

2. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391(b), (c), (d), and 15 U.S.C. §§ 15, 22.

*THE PARTIES*

3. Plaintiff MedImmune, by and through its undersigned attorneys, brings this action under antitrust, patent, and unfair competition laws against defendants Genentech, CHNMC and Celltech (collectively, "Defendants") seeking to challenge an illegal and anticompetitive agreement between Genentech and Celltech to secure the issuance of an invalid and unenforceable patent. MedImmune seeks declaratory relief that the patent is invalid, unenforceable and/or not infringed by MedImmune's Synagis® product and that MedImmune owes no payments under license agreements with Genentech.

4. MedImmune is a Delaware corporation with its principal place of business in Gaithersburg, Maryland. MedImmune uses biotechnology to develop and produce antibody therapies.

5. MedImmune's most successful product, Synagis®, is used for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus ("RSV") in pediatric patients at high risk of RSV disease. RSV infection can be fatal in certain high-risk pediatric patients.

6. Defendant Genentech is a Delaware corporation with its principal place of business in South San Francisco, California.

7. Defendant CHNMC is a California non-for-profit organization with its principal place of operation in Duarte, California. CHNMC is an assignee of the patent at issue in this case.

8. Upon information and belief, Celltech is a British company with its principal place of business in Slough, England. Through an intermediary, the Medical Research Counsel, Celltech sub-licensed MedImmune to use the technology patented in U.S. Patent No. 4,816,397 (the "Boss Patent").

*SUMMARY OF THIS ACTION*

9. MedImmune has filed this action to challenge an illegal and anticompetitive agreement (the "Agreement") between Genentech and Celltech, two large biotechnology companies, which has the effect of creating a 29-year patent monopoly over what Genentech now claims is the "fundamental technology" required for the artificial synthesis of antibody molecules. MedImmune likewise seeks a declaration that the patent improperly created by this Agreement is invalid, unenforceable and/or not infringed by MedImmune's sale of its antibody product, Synagis®, and that MedImmune owes no payments under license agreements with Genentech.

10. Genentech and Celltech have conceded the existence of the Agreement but to date have refused to make it public. Their refusal to disclose the Agreement is purportedly based on confidentiality grounds, notwithstanding the fact that the alleged "invention" at issue is already twenty years old and is described in issued patents. Nonetheless, the parties' own press releases and public filings about the terms of the Agreement have demonstrated its collusive nature and the fact that it benefits only Celltech and Genentech, while harming competition.

11. The Agreement between Celltech and Genentech was reached in the context of a dispute that began in the United States Patent and Trademark Office ("PTO") between Genentech and Celltech regarding priority of invention. Simply put, Genentech asserted that its assignors had invented the same subject matter claimed by the Boss Patent before Celltech's assignors. Thus, Genentech asserted that the Boss Patent held by Celltech (which had been in effect since 1989) should never have issued and that, instead, a new patent should be granted to Genentech covering this same technology. At the time the Agreement was entered into, the PTO had already rejected Genentech's assertion that it, and not Celltech, was entitled to a patent after conducting an administrative proceeding, known as an interference, that lasted seven years. Additionally, a federal court that considered Genentech's appeal had already rejected Genentech's attempts to obtain summary judgment in its favor.

12. Notwithstanding Celltech's legal victories over Genentech in this controversy, some time prior to March 16, 2001 Celltech and Genentech entered into the Agreement, pursuant to which (a) Genentech was declared the winner of the legal dispute between them and awarded priority of invention; (b) the PTO would immediately be asked to revoke Celltech's Boss Patent; and (c) the PTO would be asked to issue simultaneously a new patent to Genentech substantially identical to the Boss Patent (the "New Cabilly Patent"), but with a fresh 17-year life.

13. By entering the Agreement, Celltech obtained more benefits than it ever could have achieved simply by prevailing in the lawsuit with Genentech. Significantly, a Celltech Annual Report revealed that Genentech agreed to provide Celltech with a "preferential" license to the New Cabilly Patent. Moreover, although Celltech agreed to an immediate revocation of its Boss Patent, upon information and belief, it suffered no monetary harm from doing so. According to a

Celltech press release, Genentech agreed to make Celltech whole for any royalties Celltech would have received had its Boss Patent remained in existence until 2006, when it was to expire. Thus, as part of the Agreement, Genentech agreed to pay Celltech, the nominal "loser" in the legal dispute, the royalties that Celltech would have received had Celltech won. Additionally, Celltech benefits to the extent that Genentech uses the New Cabilly Patent to harm competitors of Celltech.

14. The Agreement thus provided Genentech with monopoly power based on a brand new patent with a full 17-year life that would enable Genentech to deny competitors access to what it asserts to be fundamental technology necessary for the production of monoclonal antibodies.

15. The Agreement has profoundly and fundamentally altered the competitive landscape in the biotechnology industry. Before the Agreement, Celltech had granted its competitors broad access to this technology by liberally licensing its Boss Patent. Upon information and belief, in reliance upon the permissive licensing policy of Celltech and the expectation that the patent would expire in 2006, numerous biotechnology companies, including MedImmune, launched research programs to develop monoclonal antibody products that potentially could provide great health benefits to society.

16. Many of these health and life-enhancing products are now in clinical trials to obtain FDA approval and are being prepared for commercialization. Genentech's New Cabilly Patent is an obstacle that can prevent these new antibody products from coming to market.

17. Genentech is thus in a position to demand a much higher royalty for use of this technology until 2018 (when the New Cabilly Patent will expire). Thus, the Agreement allows Genentech to exclude competitors from the market until 2018 or reap monopoly profits from any licenses which it may

choose to grant. Celltech also benefits from this state of affairs because it has "preferential access" to the New Cabilly Patent and to the extent that the New Cabilly Patent may be used to exclude firms that compete with Celltech.

18. With its New Cabilly Patent in hand, Genentech immediately exercised its illegally obtained monopoly by advising MedImmune that the New Cabilly Patent covers MedImmune's Synagis® product. As a consequence of this assertion, MedImmune began to make and continues to make significant payments to Genentech under an agreement entered into by MedImmune and Genentech on or about June 5, 1997 (the "1997 License Agreement"). This 1997 license Agreement provided rights to various intellectual property, including the patent application that later matured into the New Cabilly Patent. After issuance of the New Cabilly Patent, MedImmune was forced to obtain additional license agreements from Genentech on or about February 7, 2003—at substantial cost—to cover seven new products that MedImmune has been developing (the "2003 License Agreements") (collectively the 1997 and 2003 License Agreements are referred to herein as the "License Agreements").

19. MedImmune now seeks relief from Genentech and Celltech for their activities in violation of Sections 1 and 2 of the Sherman Act, Section 16720 of the California Cartwright Act, Section 17200 of the California Business & Professions Code, and under the common law of unjust enrichment in connection with the illegal and anticompetitive Agreement.

20. MedImmune also seeks a declaration that: (a) the New Cabilly Patent (which is co-owned by Genentech and CHNMC) is invalid; (b) the New Cabilly Patent is unenforceable; (c) MedImmune's sales of its Synagis® product do not infringe any valid claim of the New Cabilly Patent and (d) MedImmune owes no payments to Genentech under the License Agreements.

## *GENENTECH AND CELLTECH REACH THEIR AGREEMENT AND CREATE THE NEW CABILLY PATENT*

21. On April 8, 1983, Shmuel Cabilly, Herbert L Heyneker, William E. Holmes, Arthur D. Riggs and Ronald B. Wetzel (collectively, the "Applicants") filed U.S. Patent Application No. 483,457 (the "Old Cabilly Application"). Upon information and belief, Shmuel Cabilly and Arthur D. Riggs were affiliated with CHNMC, while Herbert L Heyneker, William E. Holmes and Ronald B. Wetzel were affiliated with Genentech. Upon information and belief, interests in this application and any subsequently issued patents were assigned to Genentech and CHNMC.

22. Based on the Old Cabilly Application, on March 28, 1989 the PTO issued U.S. Patent No. 4,816,567 (the "Old Cabilly Patent") to the above named Applicants.

23. On June 10, 1988 the Applicants filed U.S. Patent Application No. 205,419 (the "New Cabilly Application") as a continuation to the Old Cabilly Application.

24. On the same day the Old Cabilly Patent was issued, March 28, 1989, Celltech was issued the Boss Patent.

25. After the Boss Patent was issued, Genentech sought to claim the purported invention of the Boss Patent as its own. Genentech therefore amended its New Cabilly Application by including claims copied from the Boss Patent, which caused the PTO Board of Patent Appeals & Interferences (the "PTO Board") to initiate an interference proceeding to determine priority of invention, *i.e.*, who was first purportedly to invent the subject matter claimed by both Celltech and Genentech.

### The Seven Year PTO Interference

26. On February 28, 1991 the PTO Board declared a patent interference between Genentech's New Cabilly Application and the Boss Patent on the basis that both claimed the same purported invention.

27. Genentech and Celltech then spent the next seven years in an adversarial interference proceeding before the PTO Board, each arguing that it was the first to make the purported invention at issue.

28. On August 13, 1998 the PTO Board held that Genentech had failed to carry its burden of proving that it was the first to make the purported invention and therefore held that Celltech's Boss Patent was entitled to priority over the New Cabilly Application.

Genentech Appeals and Discovers "New" Evidence

29. Faced with its loss before the PTO Board, on October 9, 1998 Genentech commenced a civil action, *Genentech, Inc. v. Celltech R & D Ltd.*, Case No. C98-3926 MMC ("Civil Action"), in the United States District Court for the Northern District of California under 35 U.S.C. § 146 to appeal the decision of the PTO Board awarding priority of invention to Celltech.

30. The Civil Action lasted for more than two years, and included extensive depositions, document production and expert disclosure.

31. More than nine years into the dispute, sometime in early 2000, Shmuel Cabilly claimed to have found—for the very first time—a draft patent application dated February 25, 1983 (the "Draft Cabilly Application") in his files in Israel that, according to Genentech, established that Cabilly and his colleagues had invented the technology a mere 30 days before the invention date accorded to the Boss Patent based on its United Kingdom Patent application filing date.

32. Based on the late and highly convenient unearthing of this allegedly critical evidence, Genentech moved the District Court for summary judgment that it should be entitled to priority of invention over Celltech. Genentech argued that because the Draft Cabilly Application contained each and

every element of the claimed invention, and was dated earlier than the Boss priority date of March 25, 1983, Genentech should be awarded priority of invention over Boss because Genentech allegedly demonstrated "conception" of the invention by no later than the date of the draft. Further, Genentech argued that it was "reasonably diligent" in preparing and filing the application, which it conceded was a legal prerequisite to being awarded priority. However, Genentech now relied on the alleged diligence of its attorneys in preparing the patent application and "constructive" reduction to practice, which was different from the theory of inventor diligence and actual reduction to practice it had argued before the PTO Board.

Motive to Collude

33. In opposing Genentech's priority argument in the Civil Action based on the Draft Cabilly Application, Celltech asserted that the draft fell short of satisfying the legal requirements for "conception" in that it did not set forth each and every element of the invention. Additionally, Celltech argued that Genentech had changed its basic theory of the case from what it asserted before the PTO Board, a tactic which is not permitted in appeals from PTO interference proceedings.

34. Genentech responded by pointing out that Celltech's March 25, 1983 United Kingdom Boss Patent application suffered from the same deficiencies, which called into question whether Celltech had actually invented the disputed technology. Separately, Genentech also moved for summary judgment that Celltech was not entitled to the March 25, 1983 priority date because of defects in the United Kingdom Boss Patent application.

35. Thus, the dispute over the Draft Cabilly Application caused each party to argue that the other was not in possession of the "invention" at issue in early 1983. This new posture raised the possibility—which MedImmune contends

is the correct outcome—that neither Genentech nor Celltech was entitled to the patent in question. Genentech and Celltech, which had waged this priority dispute for nine years, should have appreciated the possibility that at the end of a protracted legal battle, neither side would end up with a valid patent. This realization provided a strong motive for the Agreement that they entered.

36. The illegal and anticompetitive Agreement was reduced to writing by Genentech and Celltech sometime after July 31, 2000, when the Court denied Genentech's motions for summary judgment. Upon information and belief, Genentech and Celltech entered into the Agreement with a bad faith intent to limit and injure competition as illustrated by the fact that the Agreement called for Celltech to concede defeat to Genentech and sacrifice the Boss Patent. Celltech did so, notwithstanding the facts that it had just defeated Genentech's summary judgment motions based on the "newly discovered" evidence, and that Celltech had established priority in the PTO after a seven-year proceeding.

37. According to publicly available statements, the Agreement required Genentech to make Celltech whole by compensating Celltech for the royalties it would have received under the Boss Patent. Such "reverse payments" (so-called because they were made by Genentech, the nominal winner in the "settlement," to Celltech, the nominal loser) thus provided Celltech all the benefits it would have received had it preserved the victory it had earned at the PTO Board.

38. Indeed, the Agreement put Celltech in a position *better* than any outcome it could have obtained in litigation. Celltech has publicly admitted that Genentech agreed to give Celltech and its products "preferential access" to Genentech's New Cabilly Patent, which could keep competitors at bay, or at a competitive disadvantage, for *twelve years longer* than Celltech's Boss Patent could have done so.

Genentech and Celltech Submit a Deficient Proposed Order to the District Court

39. The parties submitted a proposed order to the District Court in order to implement their Agreement. The proposed order contained a "finding" that Genentech won the priority controversy *as a matter of law* because the Draft Cabilly Application constituted evidence of "conception" prior to the Boss Patent. In fact, as Celltech had argued successfully in opposition to Genentech's summary judgment motion, the Draft Cabilly Application did no such thing in that it was missing certain key elements of the claimed invention. Having first convinced the Court that the Draft Cabilly Application did not prove conception as a matter of law, Celltech reversed course completely and asked the Court to find that it did.

40. Moreover, the findings in the proposed order were insufficient as a matter of law to declare Genentech the prevailing party. In addition to the requirement that Genentech show "conception" before the Boss priority date, it also was necessary as a matter of well established patent law for Genentech to show "reasonable diligence" during the critical period in order to pre-date the Boss Patent. Despite the fact that both Celltech and Genentech recognized and briefed this legal requirement in connection with the summary judgment motions, the proposed order contained no finding with respect to the essential requirement of "reasonable diligence." Moreover, Celltech's concession was flatly inconsistent with Celltech's previous argument that Genentech was precluded from relying on its proffered theory of "attorney diligence," having failed to raise this issue in the PTO interference proceeding.

41. Other than striking the word "proposal" in the title, the District Court on March 16, 2001 signed without change the proposed order that the parties had submitted jointly in

order to implement their illegal and anticompetitive Agreement (the "Order").

42. The March 16, 2001 Order (drafted by Genentech and Celltech) remanded the case back to the PTO Board for further action consistent with the Agreement. Specifically, the Order directed the PTO Board to do three things: (a) "to vacate the PTO's decision in *Cabilly, et al. v. Boss et al.*, Patent Interference No. 102,572"; (b) "to revoke and vacate United States Patent No. 4,816,397, issued March 28, 1989 to Boss, et al."; and (c) "to grant and issue to Genentech's Inventors (with Genentech as the assignee), *with the issue date being the same as the date of revocation of United States Patent No. 4,816,397* [the Boss Patent], a United States patent . . ." (Emphasis added).

PTO Board Expresses Concerns Regarding the Agreement

43. In response to the District Court's Order, the PTO Board revoked the Boss Patent, but refused to issue the New Cabilly Patent, noting that neither the parties nor the District Court had any authority to compel the PTO to issue a patent, particularly when the administrative examination process had not been completed.

44. The fact that the Agreement called for the instantaneous issuance of the New Cabilly Patent, when the parties well knew that the examination process had not been completed, is further evidence of their bad faith and their intent to prevent the PTO from examining the patentability of the alleged invention.

45. The PTO Board expressed concerns about the parties' Agreement. Among other things, the PTO Board noted that the Agreement effectively created a 29-year patent "We will note that if a patent is issued to Cabilly, its term will begin to run now and the public has already been subject to patent rights of Boss since 1989, and that the interference has been pending since 1991."

46. Additionally, the PTO Board expressed concern that Celltech had seemingly abandoned a winning position. In particular, there was no indication that Celltech had raised with the District Court the issue of whether Genentech's "newly discovered" Draft Cabilly Application should have been precluded from evidence because Genentech had not shown that it was diligent in locating this evidence during the more than seven year interference proceeding before the PTO Board.

47. In response to the PTO's refusal to issue the New Cabilly Patent to Genentech at the same time it revoked the Boss Patent, *Celltech* filed a new federal court action in the United States District Court for the Northern District of California seeking an order directing the PTO to issue a patent to *Genentech*. Thus, it appears that Celltech claimed to be aggrieved by the failure of the PTO to issue a patent to Genentech. Because of the Agreement, however, Celltech's concern was understandable: Not only had Genentech agreed to make Celltech whole for any "lost" royalties from the Boss Patent, but Genentech had also agreed to give Celltech "preferential access" to its New Cabilly Patent; thus, it was now in Celltech's interest to have the New Cabilly Patent issue so that it could jointly dominate the market with Genentech.

Examination of the New Cabilly Application

48. Despite its stated reservations, the PTO Board referred the New Cabilly Application to the examiner, given that a major impediment to the issuance of the patent (namely, the Boss Patent) had now been removed by the Court Order (drafted by Genentech and Celltech) resolving the priority issue.

49. During examination of the New Cabilly Application, while under a duty of candor to the PTO, Genentech engaged in improper conduct by deluging the examiner with a stack of

potentially relevant prior art references and other materials, without directing the examiner to those of most direct relevance. This practice had the effect of "burying" the most relevant prior art. Moreover, Genentech either mischaracterized or failed to cite other important prior art.

50. Genentech also should have, but did not, bring to the PTO's attention the fact that Genentech had previously taken a position about one or more prior art references that contradicted the position that Genentech was then taking before the examiner in order to attempt to obtain issuance of the New Cabilly Patent.

51. For example, Genentech had submitted to the European Patent Office ("EPO") a document in a Notice of Opposition proceeding (EP-B-0120694 (84301996.9)) filed on April 19, 1994 wherein Genentech conveyed a position regarding the significance of *Valle at* [*sic*] *al.*, 300 NATURE 71 (1982) that was contradictory to the position Genentech conveyed to the PTO regarding the significance of that same reference.

52. Had Genentech alerted the PTO to the existence of its earlier position before the EPO when it notified the PTO of the existence of the *Valle* reference, the examiner would have determined that the *Valle* prior art reference is a material reference that anticipates or renders obvious the New Cabilly Patent.

53. Moreover, Genentech attempted, by the express terms of the Agreement, to bypass the examination process altogether by requiring immediate issuance of the New Cabilly Patent. When the PTO Board rebuffed this attempt and referred the matter to the examiner, Genentech was under a duty of candor to disclose to the examiner the significant, material issues as to the patentability of the invention which became known to Genentech no later than during the course of the summary judgment briefing in the Civil Action. Not-

withstanding this duty of candor, Genentech never directed the examiner to these significant patentability issues. Properly considered by a reasonable examiner, these flaws in the so-called "invention" would have been material to the consideration of the examiner and would have resulted in a determination that the claims of the New Cabilly Application were unpatentable.

Issuance of the New Cabilly Patent

54. Subsequent to Genentech's misrepresentations and material omissions to the PTO, the New Cabilly Patent, U.S. Patent No. 6,331,415B1, issued on December 18, 2001.

55. The New Cabilly Patent is titled "Methods of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein." It lists as inventors Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs and Ronald B. Wetzel and Genentech as the assignee. A Certificate of Correction issued by the PTO on June 25, 2002 added CHNMC as an additional assignee.

56. The New Cabilly Patent purports to cover "processes for producing an immunoglobulin or an immunologically functional immunoglobulin fragment . . . in a single [host] cell" and, according to Genentech's press release, purportedly relates to the "fundamental methods and compositions used to produce antibodies by recombinant DNA technology." When injected into humans, these antibody molecules (sometimes referred to as "immunoglobulins) can help prevent disease.

57. On the same day the New Cabilly Patent was issued, Celltech issued a press release revealing some of the terms of its illegal and anticompetitive Agreement with Genentech. Celltech admitted that "Celltech will be compensated by Genentech in terms of income from sales of products which would have been covered by the Boss Patent until its normal expiring date in 2006." Thus, notwithstanding the fact that the Boss patent was revoked by the PTO Board in 2000 (pursuant

to the Agreement of the parties), upon information and belief, Celltech effectively continues to receive royalties until 2006. Receipt of royalties after patent expiration constitutes *per se* patent misuse.

58. Moreover, the Celltech press release notes that Celltech is to receive favored treatment under the New Cabilly Patent. The release says that "Celltech also . . . secured preferential access for its development programes to the Cabilly patent, which covers the production of a broad range of antibody or antibody fragment products, for its 17 year life." However, the parties have not disclosed the precise terms of this "preferential access."

Secrecy and Potentially Improper Filing of Agreement with the PTO

59. Pursuant to 35 U.S.C. § 135(c), any agreement to settle a patent interference proceeding must be filed with the PTO. As the Senate Report related to this legislation explains, "[i]nterference proceedings may be terminated in a manner hostile to the public interest by using patent interference settlement agreements as a means of restricting competition. To make such a practice more difficult the bill requires the filing of such agreements in the Patent Office." Defendants have filed the document under seal, preventing MedImmune and the public from determining the exact terms of the Agreement or even if it was filed within the prescribed time limits. A failure to file an agreement terminating an interference within the prescribed limits will result in a finding that the patent is permanently unenforceable.

60. In a letter dated February 13, 2002, MedImmune requested a copy of the Agreement from Genentech.

61. Genentech denied MedImmune's request for a copy of the Agreement in a letter dated March 24, 2002, stating that "the settlement agreement is a confidential document, and we cannot provide it to you."

62. On May 8, 2002, MedImmune petitioned the PTO for access to this Agreement, and on July 22, 2002, continuing in their efforts to conceal the Agreement from public scrutiny, both Celltech and Genentech opposed MedImmune's petition. To the best of MedImmune's knowledge, the PTO has not yet ruled on MedImmune's request as of the date of this Complaint.

*GENENTECH REAPS THE BENEFIT OF THE NEW CABILLY PATENT MONOPOLY*

63. In public statements Genentech has taken the position that the New Cabilly Patent is extremely broad. For example, Genentech's vice president of intellectual property, Sean Johnston, has stated "we do not believe that the claims are limited by type of antibody (murine, humanized [90% human sequence] or human) or by host cell type" and that "the recently issued patent broadly covers the co-expression of immunoglobulin heavy and light chain genes in a single host cell." In other words, Genentech asserts that the New Cabilly Patent broadly covers the basic method of artificially producing any monoclonal antibody using recombinant DNA technology in any type of host cell.

64. Consistent with this position, in a letter dated January 7, 2002, Genentech advised MedImmune of its "expectation that MedImmune will pay royalties on sales of its Synagis® antibody product pursuant to the license granted by Genentech under the recently issued U.S. Patent No. 6,331,415 [the New Cabilly Patent]."

65. In a letter dated February 13, 2002, MedImmune disputed this demand for royalty payment and requested an explanation of Genentech's "basis for believing that MedImmune's product would infringe any valid claim of the [New Cabilly] Patent such that royalties would be due" and also requested a copy of the Agreement.

66. Receiving no response to its February 13, 2002 letter and fearing the commencement of patent infringement litigation by Genentech before MedImmune could complete its investigation as to the validity and/or enforceability of the New Cabilly Patent, MedImmune made the requested royalty payment, but in a letter dated March 8, 2002 stated that "[s]uch payment, however, was made under protest and with reservation of all of our rights." MedImmune continues to make such royalty payments on a quarterly basis.

*INJURY TO MEDIMMUNE AND COMPETITION*

67. The Agreement substantially and adversely affects MedImmune in particular and competition in the biotechnology industry in general by limiting access to what Genentech now claims is the core technology for the production of artificially synthesized antibodies.

68. Prior to the Agreement, Celltech controlled this technology through its interest in the Boss Patent, and had authorized the Medical Research Council in London ("MRC") to grant sublicenses to the Boss Patent, which it did liberally and with minimal field of use restrictions.

69. Upon information and belief, MedImmune was one of many biotechnology companies that obtained a sublicense to the Boss Patent at a previously established royalty rate.

70. However, the Agreement effectively nullified the sublicenses freely granted by MRC to technology that would lose patent protection in 2006, and now leaves companies at the mercy of Genentech to acquire new licenses to the New Cabilly Patent, a patent which will not expire until 2018.

71. Genentech is in a position to use the New Cabilly Patent to force biotechnology companies, including MedImmune, to pay substantial royalties to retain access to the same technology that Celltech (through MRC) had once licensed to them, or simply be denied access altogether.

72. The New Cabilly Patent has damaged MedImmune in the form of the payments to Genentech under the 1997 License Agreement based on sales of Synagis®. (In addition to payments to Genentech on account of the New Cabilly Patent, MedImmune continues to pay royalties to MRC despite revocation of the Boss Patent because the Boss Patent license was part of a package with another patent.) Additionally, MedImmune has, as a practical matter, been compelled—at great cost—to enter into the 2003 License Agreements with Genentech to protect its investments in seven critically important products in various stages of preclinical and clinical trials, including the antibodies Vitaxin and Medi-507, and antibodies against each of EphA2, IL-9, PC-Cell-Derived Growth Factor ("PCDGF), Human Aspartyl (Asparaginyl) BetaHydroxylase ("HAAH"), and Human Metapneumovirus ("hMPV"), which target, among other illnesses, cancer, asthma and other respiratory diseases, rheumatoid arthritis and psoriasis. These substantial payment obligations to Genentech under the License Agreements, on account of the New Cabilly Patent, harm MedImmune's ability to compete in its sale of antibody products.

Relevant Market

73. The relevant market is the fundamental recombinant DNA technology for producing antibodies, including the process for producing an immunoglobulin or an immunologically functional immunoglobulin fragment in a single host cell that is purportedly covered by the claims of the New Cabilly Patent.

74. This technology, as interpreted by Genentech, is an essential component to the commercial manufacture of monoclonal antibodies. Upon information and belief, there is no known commercially viable method for recombinantly producing therapeutic antibody molecules without this technology, assuming that the New Cabilly Patent is as broad as Genentech says it is. If so, upon information and belief, no

known proven alternative to this technology exists currently, and the development of any such alternative would require substantial investment of money, resources and time, and cannot reasonably be expected in the foreseeable future.

75. The relevant geographic market is the entire United States.

Market Effects

76. The unlawful conduct of Genentech and Celltech has required MedImmune and, upon information and belief, other users of this technology to obtain new licenses and/or pay additional and substantial royalties under extant licenses for a term beyond that contemplated under existing patent law, or to be excluded from use of this technology.

77. The unlawful conduct of Genentech and Celltech and the resulting issuance of the New Cabilly Patent has diminished the incentive of MedImmune and other users of the technology to invest in products making use of the technology.

*FIRST CAUSE OF ACTION:*

*DECLARATORY JUDGMENT ON CONTRACTUAL RIGHTS AND OBLIGATIONS*

(Against Genentech)

78. MedImmune incorporates the allegations of paragraphs 1 through 77 as if fully set forth herein.

79. An actual controversy has arisen and now exists between the parties concerning the rights and obligations of MedImmune under the terms of the License Agreements. Genentech has demanded that MedImmune make payments under the 1997 License Agreement on the basis that Synagis® would infringe a valid claim of the New Cabilly Patent but for the 1997 License Agreement. MedImmune disputes its obligation to make payments under the 1997

License Agreement because MedImmune's sale of its Synagis® product does not infringe any valid claim of the New Cabilly Patent. The basis for invalidity of the New Cabilly Patent arises under the patent laws of the United States, 35 U.S.C. §§ 101, 102, 103, 112, *et seq.* and/or the judicially created doctrine of obviousness type double patenting.

80. MedImmune hereby seeks a declaratory judgment that it owes no payments under the License Agreements.

*SECOND CAUSE OF ACTION:*

*PATENT INVALIDITY*

(Against Genentech and CHNMC)

81. Medimmune incorporates the allegations of paragraphs 1 through 80 as if fully set forth herein.

82. An actual controversy has arisen and now exists between the parties concerning the validity of the New Cabilly Patent.

83. The New Cabilly Patent is invalid because it is anticipated and/or obvious under 35 U.S.C. §§ 102 and/or 103.

84. The New Cabilly Patent is invalid based on the judicially created doctrine of obviousness type double patenting and/or under 35 U.S.C. §§ 101 and/or 103.

85. The New Cabilly Patent is invalid under 35 U.S.C. § 112.

86. MedImmune hereby seeks a declaratory judgment that the New Cabilly Patent is invalid under 35 U.S.C. §§ 101, 102, 103, 112, *et seq.* and/or under the judicially created doctrine of obviousness type double patenting.

*THIRD CAUSE OF ACTION:*

*PATENT UNENFORCEABILITY*

(Against Genentech and CHNMC)

87. MedImmune incorporates the allegations of paragraphs 1 through 86 as if fully set forth herein.

88. An actual controversy has arisen and now exists between the parties concerning the enforceability of the New Cabilly Patent.

89. The New Cabilly Patent is unenforceable due to the patent applicants' inequitable conduct before the PTO. Such conduct included the hiding of critical references by "burying" them in the midst of other references of minimal relevance, failing to cite certain prior art at all or to act with candor regarding the significance of certain prior art, and failing to advise the PTO of previous positions that Genentech had taken with respect to certain prior art which are inconsistent with the positions it then took with respect to that same prior art before the examiner of the New Cabilly Patent. In addition, the inequitable conduct also included the failure to direct the PTO to significant flaws in the patentability of the invention which Genentech became aware of no later than during the course of the Civil Action.

90. MedImmune hereby seeks a declaratory judgment that the New Cabilly Patent is unenforceable.

*FOURTH CAUSE OF ACTION:*

*NON-INFRINGEMENT*

(Against Genentech and CHNMC)

91. MedImmune incorporates the allegations of paragraphs 1 through 90 as if fully set forth herein.

92. An actual controversy has arisen and now exists between the parties concerning whether MedImmune's

Synagis® product infringes any valid and enforceable claim of the New Cabilly Patent, but for the 1997 License Agreement.

93. MedImmune hereby seeks a declaratory judgment that, but for the 1997 License Agreement, its Synagis® product does not infringe any valid and enforceable claim of the New Cabilly Patent

*FIFTH CAUSE OF ACTION:*

*SECTION 1 OF THE SHERMAN ACT*

(Against Genentech and Celltech)

94. MedImmune incorporates the allegations of paragraphs 1 through 93 as if fully set forth herein.

95. Genentech and Celltech conspired and reached the collusive Agreement that ultimately led to the improper issuance of the New Cabilly Patent.

96. Upon information and belief, the Agreement was entered into with the bad faith intent to harm competition.

97. The Agreement has a direct effect upon interstate trade or commerce.

98. Due to Genentech's and Celltech's anticompetitive behavior, MedImmune, among others in the industry, has been harmed by either being blocked from the market altogether or by being required to make exorbitant payments for use of the technology purportedly covered by the claims of the New Cabilly Patent.

99. The unlawful contact, combination, or conspiracy of Genentech and Celltech has no legitimate business objective and is a *per se* violation of Section 1 of the Sherman Act, 15 U.S.C. § 1, *et seq.*

100. Upon information and belief, among other things, the Agreement is a market allocation agreement between horizontal competitors that is anticompetitive and illegal *per se* under Section 1 of the Sherman Act, 15 U.S.C. § 1, *et seq.*

101. Alternatively, the unlawful contract, combination, or conspiracy of Genentech and Celltech unreasonably restrains competition in the relevant market and violates Section 1 of the Sherman Act under the Rule of Reason.

102. Genentech and Celltech are liable under Section 1 of the Sherman Act to MedImmune for damages in an amount to be proven at trial, including, without limitation, all payments made by MedImmune to Genentech on account of the New Cabilly Patent; which damages should be trebled under 15 U.S.C. § 15(a), plus interest costs and expenses, including attorney fees.

*SIXTH CAUSE OF ACTION:*

*SECTION 2 OF THE SHERMAN ACT*

*(CONSPIRACY TO MONOPOLIZE)*

(Against Genentech and Celltech)

103. MedImmune incorporates the allegations of paragraphs 1 through 102 as if fully set forth herein.

104. Genentech and Celltech conspired and reached the collusive Agreement that ultimately led to the improper issuance of the New Cabilly Patent

105. Upon information and belief, the Agreement was entered into with the specific intent to grant a monopoly to Genentech that consists of the exclusive rights to what is asserted to be the fundamental technology embodied in the New Cabilly Patent

106. The Agreement has a direct effect upon interstate trade or commerce.

107. Due to Genentech's and Celltech's anticompetitive behavior, MedImmune, among others in the industry, has been harmed by either being blocked from the market altogether or by being required to make exorbitant payments for use of the technology purportedly covered by the claims of the New Cabilly Patent.

108. The unlawful conspiracy of Genentech and Celltech violates Section 2 of the Sherman Act, 15 U.S.C. § 2, *et seq.*

109. Genentech and Celltech are liable under Section 2 of the Sherman Act to MedImmune for damages in an amount to be proven at trial, including, without limitation, all payments made by MedImmune to Genentech on account of the New Cabilly Patent; which damages should be trebled under 15 U.S.C. § 15(a), plus interest, costs and expenses, including attorney fees.

*SEVENTH CAUSE OF ACTION:*

*SECTION 2 OF THE SHERMAN ACT*

*(MONOPOLIZATION BY GENENTECH)*

(Against Genentech)

110. MedImmune incorporates the allegations of paragraphs 1 through 109 as if fully set forth herein.

111. Upon information and belief, Genentech has monopoly power in the relevant market (as defined above).

112. Upon information and belief, Genentech willfully acquired and/or maintained its market dominance in the relevant market by anticompetitive means.

113. Genentech's willful acquisition and/or maintenance of its monopoly power by anticompetitive means has harmed MedImmune, among others in the industry, by either blocking them from the market altogether or requiring them to make exorbitant payments for use of the technology.

114. Genentech is liable under Section 2 of the Sherman Act to MedImmune for damages in an amount to be proven at trial, including, without limitation, all payments made to date by MedImmune to Genentech on account of the New Cabilly Patent; which damages should be trebled under 15 U.S.C. § 15(a), plus interest, costs and expenses, including attorney fees.

*EIGHTH CAUSE OF ACTION:*

*THE CARTWRIGHT ACT*

*(UNLAWFUL RESTRAINT OF TRADE)*

(Against Genentech and Celltech)

115. MedImmune incorporates the allegations of paragraphs 1 through 114 as if fully set forth herein.

116. Genentech and Celltech improperly conspired and reached the collusive Agreement that ultimately led to the improper issuance of the New Cabilly Patent

117. Upon information and belief, the Agreement was entered into with the bad faith intent to harm competition.

118. The Agreement has a direct effect upon trade or commerce in California.

119. The collusive Agreement has no legitimate pro-competitive business objective and unreasonably harms competition.

120. Due to Genentech's and Celltech's anticompetitive behavior in violation of Section 16720 of the California Cartwright Act, MedImmune has been damaged by, for example, being required to make exorbitant payments for use of the New Cabilly Patent technology. Genentech and Celltech are liable to MedImmune for damages in an amount to be proven at trial; trebled under § 16750, plus interest, costs and expenses, including attorney fees.

*NINTH CAUSE OF ACTION:*

*THE CARTWRIGHT ACT*

*(CONSPIRACY TO MONOPOLIZE)*

(Against Genentech and Celltech)

121. MedImmune incorporates the allegations of paragraphs 1 through 120 as if fully set forth herein.

122. Genentech and Celltech conspired and reached the collusive Agreement that ultimately led to the improper issuance of the New Cabilly Patent.

123. Upon information and belief, the Agreement was entered into with the specific intent to grant a monopoly to Genentech that consists of the exclusive rights to what is asserted to be the fundamental technology embodied in the New Cabilly Patent.

124. The Agreement has a direct effect upon trade or commerce in California.

125. Due to Genentech's and Celltech's anticompetitive behavior, MedImmune, among others in the industry, has been harmed by either being blocked from the market altogether or by being required to make exorbitant payments for use of the technology purportedly covered by the claims of the New Cabilly Patent.

126. The unlawful conspiracy of Genentech and Celltech violates Sections 16720 *et seq.* of the California Cartwright Act.

127. Genentech and Celltech are liable under Section 16720 of the Cartwright Act to MedImmune for damages in an amount to be proven at trial, including, without limitation, all payments made to date by MedImmune to Genentech on account of the New Cabilly Patent; which damages should be trebled under § 16720, plus interest, costs and expenses, including attorney fees.

*TENTH CAUSE OF ACTION:*

*SECTION 17200 OF THE CALIFORNIA BUSINESS & PROFESSIONS CODE*

(Against Genentech and Celltech)

128. MedImmune incorporates the allegations of paragraphs 1 through 127 as if fully set forth herein.

129. Upon information and belief, Genentech and Celltech have colluded to obtain the issuance of the New Cabilly Patent, and have engaged in unfair, illegal or fraudulent business practices in violation of Section 17200 of the California Business & Professions Code. Due to the Defendants' unfair business practices, MedImmune has been required to make exorbitant payments for use of the New Cabilly Patent's technology.

130. Genentech and Celltech are liable to MedImmune for restitution of payments made to Genentech on account of the New Cabilly Patent, which payments are continuing, and Genentech should be enjoined from attempting to enforce the New Cabilly Patent and any of the terms of the collusive Agreement.

*ELEVENTH CAUSE OF ACTION:*

*UNJUST ENRICHMENT*

(Against Genentech)

131. MedImmune incorporates the allegations of paragraphs 1 through 130 as if fully set forth herein.

132. As a result of the Agreement and improper issuance of the New Cabilly Patent, Genentech has been unjustly enriched in an amount to be proven at trial on account of payments made by MedImmune under the New Cabilly Patent, which payments are continuing.

*PRAYER FOR RELIEF*

WHEREFORE, plaintiff MedImmune requests that judgment be entered in favor of MedImmune and against Defendants:

1. DECLARING that MedImmune has no obligation to pay royalties to Genentech under the License Agreements because the New Cabilly Patent is invalid and/or unenforceable and/or because MedImmune's sale of its Synagis® product does not infringe any valid claim of the New Cabilly Patent;

2. DECLARING that the New Cabilly Patent is invalid under 35 U.S.C. §§ 101, 102, 103, 112, *et seq.* and/or the judicially created doctrine of obviousness type double patenting;

3. DECLARING that MedImmune's sale of its Synagis® product does not infringe any valid and enforceable claim of the New Cabilly Patent;

4. DECLARING that the Agreement between Genentech and Celltech violates Section 1 of the Sherman Act;

5. DECLARING that the Agreement between Genentech and Celltech violates Section 2 of the Sherman Act;

6. DECLARING that the Agreement between Genentech and Celltech violates Section 17200 of the California Business & Professions Code;

7. DECLARING that the Agreement between Genentech and Celltech violates Section 16720 of the Cartwright Act;

8. ENJOINING Genentech and/or CHNMC from enforcing the New Cabilly Patent;

9. AWARDING MedImmune damages resulting from Genentech's unjust enrichment;

10. AWARDING MedImmune actual and exemplary damages resulting from Genentech's and Celltech's anti-competitive use of the New Cabilly Patent, including, without limitation, treble damages under 15 U.S.C. § 15(a), Section 16750 of the California Cartwright Act, and such other exemplary damages as are available at law, including those available on account of Genentech's and Celltech's oppression, fraud, or malice; attorney fees; and costs; and

11. PROVIDING MedImmune such other and further relief as the Court may deem just and proper under the circumstances.

Date: April 11, 2003

DEWEY BALLANTINE LLP

By: /s/ Jeffrey R. Witham
JEFFREY R. WITHAM
Attorneys for Plaintiff MEDIMMUNE, INC.

DEMAND FOR JURY TRIAL

Plaintiff Medimmune, Inc. hereby demands a jury trial as provided by Rule 38(a) of the Federal Rules of Civil Procedure.

DEWEY BALLANTINE LLP

By: /s/ Jeffrey R. Witham
JEFFREY R. WITHAM
Attorneys for Plaintiff MEDIMMUNE, INC.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

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Case No. CV 03-02567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC, CITY OF HOPE NATIONAL MEDICAL CENTER, AND CELLTECH R&D LTD.,

*Defendants.*

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# CELLTECH R&D LTD'S ANSWER

# DEMAND FOR JURY TRIAL

Defendant Celltech R&D Ltd. ("Celltech") hereby answers the Complaint of MedImmune, Inc. ("MedImmune") and alleges as follows:

## Jurisdiction and Venue

1. Celltech admits that the Complaint purports to state a claim for declaratory relief pursuant to Fed. R. Civ. P. 57 and 28 U.S.C. §§ 2201 and 2202. Celltech further admits that it filed a complaint in the United States District Court for the Northern District of California captioned *Celltech R&D Ltd. v. Genentech, Inc.*, Civ. Act. 01-3560 JCS. Celltech admits, on information and belief, that Genentech, Inc. ("Genentech") has its principal place of business in South San Francisco, California. Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments concerning the principal place of business and place of organization of City of Hope National Medical Center ("City of Hope"). Celltech denies all other averments of Paragraph 1, except that inasmuch as the averments of jurisdiction

purport to state legal conclusions, no response thereto is required.

2. Celltech denies the averments of Paragraph 2, except that inasmuch as the averments of venue purport to state legal conclusions, no response thereto is required.

The Parties

3. Celltech admits that the Complaint purports to state claims under the cited legal theories, but denies that Plaintiff is entitled to any relief under those causes of action. Celltech denies all other averments of Paragraph 3, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

4. Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 4, and on that basis denies those averments.

5. Celltech admits that Plaintiff sells a product under the name Synagis. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 5, and on that basis denies those averments.

6. Celltech admits on information and belief that Genentech is a Delaware corporation with its principal place of business in South San Francisco, California.

7. Celltech admits that U.S. Patent No. 6,331,415 B1 states that City of Hope of Duarte, California is an assignee of the patent. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 7, and on that basis denies those averments.

8. Celltech admits that it is a British company with its principal place of business at 208 Bath Road, Slough, Berkshire, SL 1 WE, United Kingdom. Celltech admits that the Medical Research Council sub-licensed to Medimmune

use of the technology patented in U.S. Patent No. 4,816,397 (the "Boss Patent").

9. Celltech admits that the Complaint includes a demand for declaratory relief, but denies that Plaintiff is entitled to any such relief. Celltech denies each and every other averment set forth in Paragraph 9.

10. Celltech admits that it entered into certain agreements with Genentech to settle a patent interference relating to the Boss Patent and U.S. Patent Application No. 205,419 (the "Cabilly Application"), and to secure for Celltech a non-exclusive license to certain rights under U.S. Patent No. 6,331,415 B1 (the "Cabilly Patent"). Celltech further admits that the details of those agreements are confidential and proprietary. Celltech denies each and every other averment set forth in Paragraph 10.

11. Celltech admits that it entered into certain agreements with Genentech to settle a patent interference relating to the Boss Patent and the Cabilly Application, and to secure for Celltech a limited license to certain rights under the Cabilly Patent. Celltech further admits that it prevailed in the patent interference (Interference No. 102,572) before the PTO Board of Patent Interferences and Appeals and that Judge Maxine M. Chesney of the United States District Court for the Northern District of California denied Genentech's motion for summary judgment in the § 146 interference proceeding that was initiated by Genentech. Celltech denies each and every other averment set forth in Paragraph 11.

12. Celltech admits that, prior to March 16, 2001, it entered into certain agreements with Genentech to settle legal proceedings relating to Boss Patent and the Cabilly Application, and to secure for Celltech a limited license to certain rights under the Cabilly Patent. Celltech denies each and every other averment set forth in Paragraph 12.

13. Celltech admits that its 2001 Annual Report states that "Celltech has secured preferential access for its development programmes to the Cabilly patent, which covers the production of a broad range of antibody or antibody fragment products, for its 17 year life." Celltech further admits that a Celltech press release dated December 18, 2001 states: "By this settlement, Celltech will be compensated by Genentech in terms of income from sales of products which would otherwise have been covered by the Boss patent until its normal expiry date in 2006." Celltech denies each and every other averment set forth in Paragraph 13.

14. Inasmuch as the averments of Paragraph 14 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 14, and on that basis denies those averments.

15. Celltech admits that Celltech and the Medical Research Council granted several licenses to the Boss patent. Celltech further admits that the original term of the Boss patent would have expired on March 28, 2006. Celltech denies each and every other averment set forth in Paragraph 15.

16. Inasmuch as the averments of Paragraph 16 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 16, and on that basis denies those averments.

17. Celltech admits that the term of the Cabilly Patent will expire in 2018. Celltech denies each and every other averment set forth in Paragraph 17.

18. Inasmuch as the averments of Paragraph 18 do not relate to Celltech, no response thereto is required. To the

extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 18, and on that basis denies those averments.

19. Celltech admits that the Complaint purports to state claims under the cited statutes and legal theories, but denies that Plaintiff is entitled to any such relief. Celltech denies each and every other averment set forth in Paragraph 19.

20. Celltech admits that the Complaint demands declaratory relief, but denies that Plaintiff is entitled to any such relief. Celltech denies each and every other averment set forth in Paragraph 20.

21. Celltech admits that U.S. Patent No. 4,816,567 states that Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel filed U.S. Patent Application No. 483,457 on April 8, 1983. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 21, and on that basis denies those averments.

22. Celltech admits that U.S. Patent No. 4,816,567 states that it issued on March 28, 1989, based on U.S. Patent Application No. 483,457. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 22, and on that basis denies those averments.

23. Celltech admits that U.S. Patent No. 6,331,415 B1 states that U.S. Patent Application 07/205,419 was filed on June 10, 1988, as a continuation of U.S. Patent Application 06/483,457. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 23, and on that basis denies those averments.

24. Celltech admits that U.S. Patent No. 4,816,567 and U.S. Patent No. 4,816,397 were both issued by the PTO on March 28, 1989.

25. Celltech admits that Genentech amended its Cabilly Application and sought to provoke an interference with the Boss patent. Celltech further admits that Patent Interference No. 102,572 was declared by the PTO on February 28, 1991. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 25, and on that basis denies those averments, except that inasmuch as the averments .purport to state legal conclusions, no response thereto is required.

26. Celltech admits that, on February 28, 1991, the PTO Board of Patent Interferences and Appeals declared Patent Interference No. 102,572 between certain claims of the Cabilly Application and the Boss Patent. Celltech denies each and every other averment set forth in Paragraph 26, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

27. Celltech admits that Patent Interference No. 102,572 was declared on February 28, 1991 and that the final decision of the PTO Board of Patent Appeals and Interferences was issued on August 13, 1998. Celltech admits that both Celltech and Genentech made arguments to the PTO Board of Patent Appeals and Interferences relating to priority of invention. Celltech denies each and every other averment set forth in Paragraph 27.

28. Celltech admits that final decision of the PTO Board of Patent Appeals and Interferences, issued on August 13, 1998, entered judgment in favor of the Celltech inventors, and refers to that decision for its content. Celltech denies each and every other averment set forth in Paragraph 28.

29. Celltech admits that, on October 9, 1998, Genentech initiated a civil action under 35 U.S.C. § 146 entitled

*Genentech, Inc. v. Celltech R&D Ltd.*, Case No. C98-3926 MMC (the "Civil Action"), in the United States District Court for the Northern District of California. Celltech denies each and every other averment set forth in Paragraph 29.

30. Celltech admits that the Civil Action was filed on October 9, 1998 and judgment was entered by the district court on March 16, 2001. Celltech admits that the Civil Action included depositions, document production, and expert disclosures. Celltech denies each and every other averment set forth in Paragraph 30.

31. Celltech admits that, during the course of the Civil Action, Genentech produced a draft patent application. Celltech admits that Genentech made certain contentions regarding the draft patent application, including statements made in Genentech's summary judgment papers filed in the Civil Action, and refers to Genentech's motion papers for their content. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 31, and on that basis denies those averments.

32. Celltech admits that Genentech moved in the Civil Action for summary judgment in its favor, and refers to Genentech's motion papers for their content. Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 32, and on that basis denies those averments, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

33. Celltech admits that it opposed Genentech's motion for summary judgment in the Civil Action, and refers to Genentech's motion papers for their content. Celltech denies each and every other averment set forth in Paragraph 33, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

34. Celltech admits that Genentech filed a reply brief in support of its motion for summary judgment, and refers to Genentech's motion papers for their content. Celltech admits that Genentech filed a motion for summary judgment that Celltech was not entitled to priority to the March 25, 1983 filing date of the United Kingdom Boss patent application, and refers to Genentech's motion papers for their content. Celltech denies each and every other averment set forth in Paragraph 34.

35. Celltech admits that summary judgment motions were filed by Genentech in the Civil Action, and refers to Genentech's motion papers for their content. Celltech denies each and every other averment set forth in Paragraph 35, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

36. Celltech admits that it entered into certain agreements with Genentech to settle a patent interference relating to the Boss Patent and the Cabilly Application, and to secure for Celltech a limited license to certain rights under the Cabilly Patent. Celltech further admits that it prevailed in the patent interference before the PTO Board of Patent Interferences and Appeals and that Judge Maxine M. Chesney of the United States District Court for the Northern District of California denied Genentech's motion for summary judgment in the § 146 interference proceeding that was initiated by Genentech. Celltech denies each and every other averment set forth in Paragraph 36.

37. Celltech denies each and every averment set forth in Paragraph 37, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

38. Celltech denies each and every averment set forth in Paragraph 38, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

39. Celltech admits that in connection with their settlement agreement, Genentech and Celltech submitted a proposed order to the District Court, and that the proposed order contained several proposed findings of fact and conclusions of law, including a proposed finding that "Genentech is entitled as a matter of law to priority over Celltech to invention described by the count." Celltech denies each and every other averment set forth in Paragraph 39, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

40. Celltech denies each and every averment set forth in Paragraph 40, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

41. Celltech admits that the District Court executed the proposed order and entered that Order on March 16, 2001, and refers to the Order for its content. Celltech denies each and every other averment set forth in Paragraph 41.

42. Celltech admits the District Court entered a Judgment in the Civil Action, and refers to the Judgment for its content. Celltech further admits that, among other things, the District Court's Judgment directed the PTO to: "vacate the PTO's decision in *Cabilly et al. v. Boss et al.*, Patent Interference No. 102,572"; "revoke and vacate United States Patent No. 4,816,397, issued March 28, 1989 to Boss *et al.*"; and "grant and issue to Genentech's Inventors (with Genentech as the assignee), with the issue date being the same as the date of revocation of United States Patent No. 4,816,397, a United States patent . . . ." Celltech denies each and every other averment set forth in paragraph 42.

43. Celltech admits that, following entry of the District Court's Judgment, the PTO Board of Patent Interferences and Appeals issued a Final Order After District Court Judgment, and refers to the Final Order for its terms. Celltech denies each and every other averment set forth in Paragraph 43.

44. Celltech denies each and every averment set forth in Paragraph 44.

45. Celltech admits that the PTO Board of Patent Interferences and Appeals' Final Order After District Court Judgment stated, in part, "[w]e will note that if a patent is issued to Cabilly, its term will begin to run now and the public has already been subject to patent rights of Boss since 1989, and that the interference has been pending since 1991." Celltech refers to the Final Order for its terms. Celltech denies each and every other averment set forth in Paragraph 45.

46. Celltech admits that the PTO Board of Patent Interferences and Appeals issued a Final Order After District Court Judgment, and refers to the Final Order for its terms. Celltech denies each and every other averment set forth in Paragraph 46.

47. Celltech admits that it commenced a civil action, *Celltech R&D Ltd. v. Genentech, Inc.*, in the United States District Court for the Northern District of California pursuant to 35 U.S.C. § 146. Celltech denies each and every other averment set forth in Paragraph 47.

48. Celltech admits the PTO Board of Patent Interferences and Appeals referred the Cabilly Application to a patent examiner. Celltech denies each and every other averment set forth in Paragraph 48.

49. Inasmuch as the averments of Paragraph 49 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 49, and on that basis denies those averments.

50. Inasmuch as the averments of Paragraph 50 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is

deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 50, and on that basis denies those averments.

51. Inasmuch as the averments of Paragraph 51 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 51, and on that basis denies those averments.

52. Inasmuch as the averments of Paragraph 52 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 52, and on that basis denies those averments.

53. Inasmuch as the averments of Paragraph 53 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 53, and on that basis denies those averments.

54. Inasmuch as the averments of Paragraph 54 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that U.S. Patent No. 6,331,415 B1, issued on December 18, 2001. Celltech is without knowledge or information sufficient to form a belief as to the truth of every other averment in Paragraph 54, and on that basis denies those averments.

55. Inasmuch as the averments of Paragraph 55 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech

admits that U.S. Patent No. 6,331,415 B1 is titled "Method of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein," and lists Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel as inventors. Celltech further admits that the patent lists Genentech as the assignee and that a Certificate of Correction issued by the PTO on June 25, 2002 added City of Hope as an additional assignee. Celltech is without knowledge or information sufficient to form a belief as to the truth of every other averment in Paragraph 55, and on that basis denies those averments.

56. Inasmuch as the averments of Paragraph 56 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that certain antibody molecules can be used to provide beneficial treatment for certain illnesses. Celltech is without knowledge or information sufficient to form a belief as to the truth of every other averment in Paragraph 56, and on that basis denies those averments.

57. Celltech admits that it issued a press release on December 18, 2001, denies that Medimrnune has accurately quoted the press release, and refers to the press release for its terms. Celltech further admits that the press release stated, in part, that "By this settlement, Celltech will be compensated by Genentech in terms of income from sales of products which would otherwise have been covered by the Boss Patent until its normal expiry date in 2006." Celltech denies each and every other averment set forth in Paragraph 57.

58. Celltech admits that it issued a press release on December 18, 2001, denies that Medlmmune has accurately quoted the press release, and refers to the press release for its terms. Celltech further admits that the press release stated, in part, that "Celltech has also secured rights to Genentech's Cabilly patent for its products." Celltech denies each and every other averment set forth in Paragraph 58.

59. Celltech admits the referenced Senate Report contains the quoted language. Celltech further admits that Celltech and Genentech filed their settlement agreement with the PTO under seal pursuant to applicable PTO rules and procedures. Celltech denies each and every other averment of Paragraph 59, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

60. Inasmuch as the averments of Paragraph 60 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 60, and on that basis denies those averments.

61. Inasmuch as the averments of Paragraph 61 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 61, and on that basis denies those averments.

62. Celltech admits that, on May 8, 2002, Plaintiff petitioned the PTO for access to Celltech's and Genentech's settlement agreement, and that Celltech and Genentech opposed that petition. Celltech further states that, on April 4, 2003, the PTO Board of Patent Interferences and Appeals rejected Plaintiff's petition, finding that the petition "appears to constitute a 'fishing expedition' that cannot be granted absent, as respondents have indicated, 'something more' constituting the requisite 'good cause.'" Celltech denies each and every other averment set forth in Paragraph 62.

63. Inasmuch as the averments of Paragraph 63 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 63, and on that basis denies those averments.

64. Inasmuch as the averments of Paragraph 64 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 64, and on that basis denies those averments.

65. Inasmuch as the averments of Paragraph 65 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 65, and on that basis denies those averments.

66. Inasmuch as the averments of Paragraph 66 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 66, and on that basis denies those averments.

67. Celltech denies each and every averment set forth in Paragraph 67.

68. Celltech admits that it owned the Boss patent. Celltech further admits that it granted to the Medical Research Council in London a license to the Boss patent, which license included the right to grant sublicenses, and refers to the sublicenses granted by Medical Research Council for their terms. Celltech denies each and every other averment set forth in Paragraph 68.

69. Celltech admits that Plaintiff, as well as several other individuals and entities, obtained a sublicense to the Boss patent. Celltech denies each and every other averment set forth in Paragraph 69.

70. Celltech denies each and every averment set forth in Paragraph 70.

71. Inasmuch as the averments of Paragraph 71 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 71, and on that basis denies those averments.

72. Inasmuch as the averments of Paragraph 72 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 72, and on that basis denies those averments.

73. Inasmuch as the averments of Paragraph 73 purport to state legal conclusions, no response thereto is required. To the extent a response is required, Celltech denies each and every averment set forth in Paragraph 73.

74. Inasmuch as the averments of Paragraph 74 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 74, and on that basis denies those averments.

75. Inasmuch as the averments of Paragraph 75 purport to state legal conclusions, no response thereto is required. To the extent a response is required, Celltech denies each and every averment set forth in Paragraph 75.

76. Celltech denies that it engaged in unlawful conduct. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 76, and on that basis denies those averments.

77. Celltech denies that it engaged in unlawful conduct. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 77, and on that basis denies those averments.

First Cause of Action
Declaratory Judgment on Contractual Rights and Obligations
(Against Genentech)

78. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 77 of this Answer as if fully set forth herein.

79. Inasmuch as the averments of Paragraph 79 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 79, and on that basis denies those averments.

80. Inasmuch as the averments of Paragraph 80 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Complaint purports to state a claim for declaratory judgment. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 80, and on that basis denies those averments.

Second Cause of Action
Patent Invalidity
(Against Genentech and City of Hope)

81. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 80 of this Answer as if fully set forth herein.

82. Inasmuch as the averments of Paragraph 82 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 82, and on that basis denies those averments.

83. Inasmuch as the averments of Paragraph 83 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 83, and on that basis denies those averments.

84. Inasmuch as the averments of Paragraph 84 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 84, and on that basis denies those averments.

85. Inasmuch as the averments of Paragraph 85 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 85, and on that basis denies those averments.

86. Inasmuch as the averments of Paragraph 86 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Complaint purports to state a claim for declaratory judgment. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 86, and on that basis denies those averments.

Third Cause of Action
Patent Unenforceability
(Against Genentech and City of Hope)

87. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 86 of this Answer as if fully set forth herein.

88. Inasmuch as the averments of Paragraph 88 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 88, and on that basis denies those averments.

89. Inasmuch as the averments of Paragraph 89 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 89, and on that basis denies those averments.

90. Inasmuch as the averments of Paragraph 90 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Complaint purports to state a claim for declaratory judgment. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 90, and on that basis denies those averments.

Fourth Cause of Action
Non-Infringement
(Against Genentech and City of Hope)

91. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 90 of this Answer as if fully set forth herein.

92. Inasmuch as the averments of Paragraph 92 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 92, and on that basis denies those averments.

93. Inasmuch as the averments of Paragraph 93 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Complaint purports to state a claim for declaratory judgment. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 93, and on that basis denies those averments.

Fifth Cause of Action
Section 1 of the Sherman Act
(Against Genentech and Celltech)

94. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 93 of this Answer as if fully set forth herein.

95. Celltech denies each and every averment set forth in Paragraph 95.

96. Celltech denies each and every averment set forth in Paragraph 96.

97. Celltech denies each and every averment set forth in Paragraph 97, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

98. Celltech denies each and every averment set forth in Paragraph 98.

99. Celltech denies each and every averment set forth in Paragraph 99, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

100. Celltech denies each and every averment set forth in Paragraph 100, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

101. Celltech denies each and every averment set forth in Paragraph 101, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

102. Celltech denies that Plaintiff is entitled to any relief under Section 1 of the Sherman Act and denies each and every other averment set forth in Paragraph 101, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Sixth Cause of Action
Section 2 of the Sherman Act (Conspiracy to Monopolize)
(Against Genentech and Celltech)

103. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 102 of this Answer as if fully set forth herein.

104. Celltech denies each and every averment set forth in Paragraph 104.

105. Celltech denies each and every averment set forth in Paragraph 105.

106. Celltech denies each and every averment set forth in Paragraph 106, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

107. Celltech denies each and every averment set forth in Paragraph 107.

108. Celltech denies each and every averment set forth in Paragraph 108, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

109. Celltech denies that Plaintiff is entitled to any relief under Section 2 of the Sherman Act and denies each and every averment set forth in Paragraph 109, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Seventh Cause of Action
Section 2 of the Sherman Act
(Against Genentech)

110. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 109 of this Answer as if fully set forth herein.

111. Inasmuch as the averments of Paragraph 111 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 111, and on that basis denies those averments.

112. Inasmuch as the averments of Paragraph 112 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 112, and on that basis denies those averments.

113. Inasmuch as the averments of Paragraph 113 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 113, and on that basis denies those averments.

114. Inasmuch as the averments of Paragraph 114 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 114, and on that basis denies those averments.

Eighth Cause of Action
The Cartwright Act (Unlawful Restraint of Trade)
(Against Genentech and Celltech)

115. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 114 of this Answer as if fully set forth herein.

116. Celltech denies each and every averment set forth in Paragraph 116.

117. Celltech denies each and every averment set forth in Paragraph 117.

118. Celltech denies each and every averment set forth in Paragraph 118, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

119. Celltech denies each and every averment set forth in Paragraph 119, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

120. Celltech denies that Plaintiff is entitled to any relief under the Cartwright Act and denies each and every other averment set forth in Paragraph 120, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Eighth Cause of Action
The Cartwright Act (Conspiracy to Monopolize)
(Against Genentech and Celltech)

121. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 120 of this Answer as if fully set forth herein.

122. Celltech denies each and every averment set forth in Paragraph 122.

123. Celltech denies each and every averment set forth in Paragraph 123.

124. Celltech denies each and every averment set forth in Paragraph 124, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

125. Celltech denies each and every averment set forth in Paragraph 125.

126. Celltech denies each and every averment set forth in Paragraph 126, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

127. Celltech denies that Plaintiff is entitled to any relief under the Cartwright Act and denies each and every averment set forth in Paragraph 127, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Tenth Cause of Action
Section 17200 of the California Business & Professions Code
(Against Genentech and Celltech)

128. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 127 of this Answer as if fully set forth herein.

129. Celltech denies each and every averment set forth in Paragraph 129, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

130. Celltech denies that Plaintiff is entitled any relief under Section 17200 and denies each and every averment set forth in Paragraph 130, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Eleventh Cause of Action
Unjust Enrichment
(Against Genentech)

131. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 130 of this Answer as if fully set forth herein.

132. Inasmuch as the averments of Paragraph 132 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 132, and on that basis denies those averments.

Affirmative Defenses

As for its further and separate defenses, Celltech states the following affirmative defenses without assuming the burden of proof on such defenses that would otherwise rest on Plaintiff.

*First Affirmative Defense*

133. The causes of action asserted in the Complaint fail to state a claim upon which relief may be granted.

*Second Affirmative Defense*

134. Plaintiff has an adequate remedy at law and no basis exists for the grant of equitable relief.

*Third Affirmative Defense*

135. Plaintiff's causes of action are barred by the Noerr-Pennington doctrine, the First Amendment and/or related doctrines.

*Fourth Affirmative Defense*

136. Plaintiff's claims are barred for failure to mitigate damages.

*Fifth Affirmative Defense*

137. Plaintiff's claims are barred to the extent that Plaintiff's purported injuries and damages were not proximately caused by any acts or omissions of Celltech.

*Sixth Affirmative Defense*

138. The Fifth, Sixth, Seventh and Eighth causes of action should be dismissed because Plaintiff has not suffered, and will not suffer, injury of the type the antitrust laws were designed to prevent.

*Seventh Affirmative Defense*

139. The equitable doctrine of unclean hands prevents the relief requested by Plaintiff.

*Eighth Affirmative Defense*

140. Any and all Celltech's conduct challenged by Plaintiff was justified, constituted bona fide business competition, and was carried out in furtherance of Celltech's legitimate business objectives.

*Ninth Affirmative Defense*

141. The Fifth, Sixth, Seventh and Eighth causes of action are barred by the U.S. patent laws.

*Tenth Affirmative Defense*

142. Plaintiff's causes of action are barred by the equitable doctrines of waiver, laches, and estoppel.

*Eleventh Affirmative Defense*

143. Plaintiff lacks standing to the bring [*sic*] causes of action asserted in the Complaint.

*Twelfth Affirmative Defense*

144. Plaintiff is barred from recovering restitution from Celltech of payments made to Genentech

Prayer for Relief

WHEREFORE, Celltech requests relief as follows:

1. That Plaintiff's claims be dismissed;
2. That Plaintiff take nothing by reason of its Complaint for Damages;
3. That Plaintiff's request for injunctive relief by denied;
4. For the cost of this suit, including reasonable attorneys' fees; and
5. For such other and further relief as the Court may deem proper.

Demand for Jury Trial

Celltech hereby demands a trial by jury for all issues so triable in this action.

Dated: June 4, 2003

LORI A. SCHECHTER
CHARLES S. BARQUIST
JASON A. CROTTY
CHRISTOPHER P. WILLARD
MORRISON & FOERSTER LLP

By: /s/ Charles S. Barquist
CHARLES S. BARQUIST

Attorneys for Defendant
CELLTECH R&D LTD.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

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Case No. CV03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC., CITY OF HOPE NATIONAL MEDICAL CENTER, and CELLTECH R&D LTD.,

*Defendants.*

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# GENENTECH, INC.'S NOTICE OF MOTION AND MOTION TO DISMISS THE THIRD AND ELEVENTH CAUSES OF ACTION; MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT

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## NOTICE OF MOTION AND MOTION

PLEASE TAKE NOTICE THAT at 10 a.m. on July 21, 2003, or as soon thereafter as the matter can be heard, before the Honorable Mariana R. Pfaelzer, in Courtroom 12 of the United States District Court for the Central District of California, Defendant Genentech, Inc. ("Genentech") will and hereby does move under Federal Rule of Civil Procedure 12(b)(6) for dismissal of plaintiff's Third Cause of Action (Patent Unenforceability) and plaintiff's Eleventh Cause of Action (Unjust Enrichment).

The motion against the Third Cause of Action will be based on the fact that the cause of action fails to state a claim on which relief can be granted because it does not plead inequitable conduct with the particularity required by Federal Rule of Civil Procedure 9(b). In addition, the cause of action

fails to state a claim under Rule 12(b)(6) because it does not allege deceptive intent. The motion against the Eleventh Cause of Action will be based on the fact that the cause of action fails to state a claim on which relief can be granted because it sounds in quasi-contract, and therefore cannot lie because express contracts define the parties' rights on the same subject matter.

This motion is based on this Notice of Motion and Motion, on the Memorandum of Points and Authorities filed concurrently herewith, on the pleadings and papers on file in this action, and on the oral argument at the hearing on the motion.

This motion is made following the conference of counsel pursuant to Local Rule 7-3 which took place on May 28, 2003.

Date: June 4, 2003

Respectfully submitted,

LATHAM & WATKINS LLP
Daniel M. Wall
Mark A. Flagel
James K. Lynch

By /s/ Mark A. Flagel
MARK A. FLAGEL
Attorneys for Defendant
Genentech, Inc.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

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Case No. CV-03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH INC., CITY OF HOPE NATIONAL MEDICAL CENTER, and CELLTECH R&D LTD.,

*Defendants.*

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# CITY OF HOPE NATIONAL MEDICAL CENTER'S NOTICE OF JOINDER AND JOINDER IN GENENTECH, INC.'S MOTION TO DISMISS THE THIRD CAUSE OF ACTION

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TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

PLEASE TAKE NOTICE that Defendant City of Hope National Medical Center ("City of Hope") hereby joins in the Motion to Dismiss the Third Cause of Action filed by defendant Genentech, Inc. ("Genentech"). City of Hope is not a defendant on plaintiff Medimmune, Inc.'s, eleventh cause of action, which Genentech also challenges in the motion.

City of Hope respectfully requests the Court to grant the motion to dismiss the third cause of action for the reasons set forth in Genentech's memorandum of points and authorities in support of the motion.

Dated: June 4, 2003 Respectfully submitted,

IRELL & MANELLA LLP
Morgan Chu
David I. Gindler
Joseph M. Lipner

By: /s/ Joseph M. Lipner
JOSEPH M. LIPNER
Attorneys for Defendant
City of Hope National Medical Center

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Aug. 11, 2003]

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Case No. CV03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC., CITY OF HOPE NATIONAL MEDICAL CENTER, and CELLTECH R&D LTD.,

*Defendants.*

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# ORDER GRANTING GENENTECH, INC.'S MOTION TO DISMISS THE THIRD AND ELEVENTH CAUSES OF ACTION

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Genentech, Inc.'s motion to dismiss the Third and Eleventh causes of action of MedImmune's Complaint came on for hearing before this Court on August 4, 2003, at 10:00 a.m. in Courtroom 12, Spring Street, with all parties having appeared through counsel.

The Court having reviewed the motion, and after consideration of the opposition and reply papers, arguments of counsel, and all other matters presented to the Court, IT IS HEREBY ORDERED THAT:

The motion is GRANTED as to the Third Cause of Action, and Plaintiff MedImmune has until August 13, 2003 to file and serve a First Amended Complaint The motion is GRANTED as to the Eleventh Cause of Action without leave to amend.

Date: Aug. 11, 2003

/s/ Mariana R. Pfaelzer
HON. MARIANA R. PFAELZER
United States District Judge

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Aug. 13, 2003]

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Case No. 03-2567 MRP (CTX)

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MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.

*Defendants.*

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PLAINTIFF MEDIMMUNE, INC'S FIRST AMENDED COMPLAINT FOR:

1. Declaratory Judgment;
2. Patent Invalidity;
3. Patent Unenforceability;
4. Non-Infringement;
5. Section 1 of the Sherman Act;
6. Section 2 of the Sherman Act;
7. The Cartwright Act;
8. Section 17200 of the Cal. Bus. & Profs. Code.

DEMAND FOR JURY TRIAL

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*JURISDICTION AND VENUE*

1. Plaintiff MedImmune, Inc. ("MedImmune") seeks declaratory relief pursuant to Fed. R. Civ. P. 57 and 28 U.S.C. §§ 2201 and 2202. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331, 1337 and 1338(a). This Court has jurisdiction over the state law claims asserted hereunderpursuant to 28 U.S.C. § 1367. This Court has personal jurisdiction over defendant Genentech, Inc. ("Genentech") based on its principal place of business in California. This

Court has personal jurisdiction over defendant City of Hope ("COH") based on its organization under the laws of the state of California and because its principal place of operation is in California. This Court has personal jurisdiction over defendant Celltech R&D Ltd. ("Celltech") based on its activities in this jurisdiction, including, but not limited to, Celltech's filing of a suit against Genentech under 35 U.S.C. § 146 in the Northern District of California captioned *Celltech R&D Ltd. v. Genentech, Inc.*, Civ. Act 01-3560JCS (N.D. Cal. 2001).

2. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391(b), (c), (d), and 15 U.S.C. §§ 15, 22.

*THE PARTIES*

3. Plaintiff MedImmune, by and through its undersigned attorneys, brings this action under antitrust, patent, and unfair competition laws against defendants Genentech, COH and Celltech (collectively, "Defendants") seeking to challenge an illegal and anticompetitive agreement between Genentech and Celltech to secure the issuance of an invalid and unenforceable patent. MedImmune seeks declaratory relief that the patent is invalid, unenforceable and/or not infringed by MedImmune's Synagis® product and that MedImmune owes no payments under license agreements with Genentech.

4. MedImmune is a Delaware corporation with its principal place of business in Gaithersburg, Maryland. MedImmune uses biotechnology to develop and produce antibody therapies.

5. MedImmune's most successful product, Synagis®, is used for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus ("RSV") in pediatric patients at high risk of RSV disease. RSV infection can be fatal in certain high-risk pediatric patients.

6. Defendant Genentech is a Delaware corporation with its principal place of business in South San Francisco, California.

7. Defendant COH is a California non-for-profit organization with its principal place of operation in Duarte, California. COH is an assignee of the patent at issue in this case.

8. Upon information and belief, Celltech is a British company with its principal place of business in Slough, England. Through an intermediary, the Medical Research Counsel, Celltech sub-licensed MedImmune to use the technology patented in U.S. Patent No. 4,816,397 (the "Boss Patent").

*SUMMARY OF THIS ACTION*

9. MedImmune has filed this action to challenge an illegal and anticompetitive agreement (the "Agreement") between Genentech and Celltech, two large biotechnology companies, which has the effect of creating a 29-year patent monopoly over what Genentech now claims is the "fundamental technology" required for the artificial synthesis of antibody molecules. MedImmune likewise seeks a declaration that the patent improperly created by this Agreement is invalid, unenforceable and/or not infringed by MedImmune's sale of its antibody product, Synagis®, and that MedImmune owes no payments under license agreements with Genentech.

10. Genentech and Celltech have conceded the existence of the Agreement but to date have refused to make it public. Their refusal to disclose the Agreement is purportedly based on confidentiality grounds, notwithstanding the fact that the alleged "invention" at issue is already twenty years old and is described in issued patents. Nonetheless, the parties' own press releases and public filings about the terms of the Agreement have demonstrated its collusive nature and the fact that it benefits only Celltech and Genentech, while harming competition.

11. The Agreement between-Celltech and Genentech was reached in the context of a dispute that began in the United States Patent and Trademark Office ("PTO" between Genentech and Celltech regarding priority of invention. Simply put, Genentech asserted that its assignors had invented the same subject matter claimed by the Boss Patent before Celltech's assignors. Thus, Genentech asserted that the Boss Patent held by Celltech (which had been in effect since 1989) should never have issued and that, instead, a new patent should be granted to Genentech covering this same technology. At the time the Agreement was entered into, the PTO had already rejected Genentech's assertion that it, and not Celltech, was entitled to a patent after conducting an administrative proceeding, known as an interference, that lasted seven years. Additionally, a federal court that considered Genentech's appeal had already rejected Genentech's attempts to obtain summary judgment in its favor.

12. Notwithstanding Celltech's legal victories over Genentech in this controversy, some time prior to March 16, 2001 Celltech and Genentech entered into the Agreement, pursuant to which (a) Genentech was declared the winner of the legal dispute between them and awarded priority of invention; (b) the PTO would immediately be asked to revoke Celltech's Boss Patent; and (c) the PTO would be asked to issue simultaneously a new patent to Genentech substantially identical to the Boss Patent (the "New Cabilly Patent"), but with a fresh 17-year life.

13. By entering the Agreement, Celltech obtained more benefits than it ever could have achieved simply by prevailing in the lawsuit with Genentech. Significantly, a Celltech Annual Report revealed that Genentech agreed to provide Celltech with a "preferential" license to the New Cabilly Patent. Moreover, although Celltech agreed to an immediate revocation of its Boss Patent, upon information and belief, it suffered no monetary harm from doing so. According to a

Celltech press release, Genentech agreed to make Celltech whole for any royalties Celltech would have received had its Boss Patent remained in existence until 2006, when it was to expire. Thus, as part of the Agreement, Genentech agreed to pay Celltech, the nominal "loser" in the legal dispute, the royalties that Celltech would have received had Celltech won. Additionally, Celltech benefits to the extent that Genentech uses the New Cabilly Patent to harm competitors of Celltech.

14. The Agreement thus provided Genentech with monopoly power based on a brand new patent with a full 17-year life that would enable Genentech to deny competitors access to what it asserts to be fundamental technology necessary for the production of monoclonal antibodies.

15. The Agreement has profoundly and fundamentally altered the competitive landscape in the biotechnology industry. Before the Agreement, Celltech had granted its competitors broad access to this technology by liberally licensing its Boss Patent. Upon information and belief, in reliance upon the permissive licensing policy of Celltech and the expectation that the patent would expire in 2006, numerous biotechnology companies, including MedImmune, launched research programs to develop monoclonal antibody products that potentially could provide great health benefits to society.

16. Many of these health and life-enhancing products are now in clinical trials to obtain FDA approval and are being prepared for commercialization. Genentech's New Cabilly Patent is an obstacle that can prevent these new antibody products from coming to market.

17. Genentech is thus in a position to demand a much higher royalty for use of this technology until 2018 (when the New Cabilly Patent will expire). Thus, the Agreement allows Genentech to exclude competitors from the market until 2018 or reap monopoly profits from any licenses which it may choose to grant. Celltech also benefits from this state of

affairs because it has "preferential access" to the New Cabilly Patent and to the extent that the New Cabilly Patent may be used to exclude firms that compete with Celltech.

18. With its New Cabilly Patent in hand, Genentech immediately exercised its illegally obtained monopoly by advising MedImmune that the New Cabilly Patent covers MedImmune's Synagis® product. As a consequence of this assertion, MedImmune began to make and continues to make significant payments to Genentech under an agreement entered into by MedImmune and Genentech on or about June 5, 1997 (the "1997 License Agreement"). This 1997 License Agreement provided rights to various intellectual property, including the patent application that later matured into the New Cabilly Patent. After issuance of the New Cabilly Patent, MedImmune was forced to obtain additional license agreements from Genentech on or about February 7, 2003—at substantial cost—to cover seven new products that MedImmune has been developing (the "2003 License Agreements") (collectively the 1997 and 2003 License Agreements are referred to herein as the "License Agreements").

19. MedImmune now seeks relief from Genentech and Celltech for their activities in violation of Sections 1 and 2 of the Sherman Act, Section 16720 of the California Cartwright Act and Section 17200 of the California Business & Professions Code in connection with the illegal and anticompetitive Agreement.

20. MedImmune also seeks a declaration that: (a) the New Cabilly Patent (which is co-owned by Genentech and COH) is invalid; (b) the New Cabilly Patent is unenforceable; (c) MedImmune's sales of its Synagis® product do not infringe any valid claim of the New Cabilly Patent; and (d) MedImmune owes no payments to Genentech under the License Agreements.

*GENENTECH AND CELLTECH REACH THEIR AGREEMENT AND CREATE THE NEW CABILLY PATENT*

21. On April 8, 1983, Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs and Ronald B. Wetzel (collectively, the "Applicants") filed U.S. Patent Application No. 483,457 (the "Old Cabilly Application"). Upon information and belief, Shmuel Cabilly and Arthur D. Riggs were affiliated with COH, while Herbert L. Heyneker, William E. Holmes and Ronald B. Wetzel were affiliated with Genentech. Upon information and belief, interests in this application and any subsequently issued patents were assigned to Genentech and COH.

22. Based on the Old Cabilly Application, on March 28, 1989 the PTO issued U.S. Patent No. 4,816,567 (the "Old Cabilly Patent") to the above named Applicants.

23. On June 10, 1988 the Applicants filed U.S. Patent Application No. 205,419 (the "New Cabilly Application") as a continuation to the Old Cabilly Application.

24. On the same day the Old Cabilly Patent was issued, March 28, 1989. Celltech was issued the Boss Patent.

25. After the Boss Patent was issued, Genentech sought to claim the purported invention of the Boss Patent as its own. Genentech therefore amended its New Cabilly Application by including claims copied from the Boss Patent, which caused the PTO Board of Patent Appeals & Interferences (the "PTO Board") to initiate an interference proceeding to determine priority of invention, *i.e.*, who was first purportedly to invent the subject matter claimed by both Celltech and Genentech.

The Seven Year PTO Interference

26. On February 28, 1991 the PTO Board declared a patent interference between Genentech's New Cabilly Application and the Boss Patent on the basis that both claimed the same purported invention.

27. Genentech and Celltech then spent the next seven years in an adversarial interference proceeding before the PTO Board, each arguing that it was the first to make the purported invention at issue.

28. On August 13, 1998 the PTO Board held that Genentech had failed to carry its burden of proving that it was the first to make the purported invention and therefore held that Celltech's Boss Patent was entitled to priority over the New Cabilly Application.

Genentech Appeals and Discovers "New" Evidence

29. Faced with its loss before the PTO Board, on October 9, 1998 Genentech commenced a civil action, *Genentech, Inc. v. Celltech R & D Ltd.*, Case No. C98-3926 MMC ("Civil Action"), in the United States District Court for the Northern District of California tinder 35 U.S.C. § 146 to appeal the decision of the PTO Board awarding priority of invention to Celltech.

30. The Civil Action lasted for more than two years, and included extensive depositions, document production and expert disclosure.

31. More than nine years into the dispute, sometime in early 2000, Shmuel Cabilly claimed to have found—for the very first time—a draft patent application dated February 25, 1983 (the "Draft Cabilly Application") in his files in Israel that, according to Genentech, established that Cabilly and his colleagues had invented the technology a mere 30 days before the invention date accorded to the Boss Patent based on its March 25, 1983 British Patent Application (the "British Patent Application") filing date.

32. Based on the late and highly convenient unearthing of this allegedly critical evidence, Genentech moved the District Court for summary judgment that it should be entitled to priority of invention over Celltech. Genentech argued that

because the Draft Cabilly Application contained each and every element of the claimed invention, and was dated earlier than the Boss priority date of March 25, 1983, Genentech should be awarded priority of invention over Boss because Genentech allegedly demonstrated "conception" of the invention by no later than the date of the draft. Further, Genentech argued that it was "reasonably diligent" in preparing and filing the application, which it conceded was a legal prerequisite to being awarded priority. However, in the Civil Action, Genentech was relying on the alleged diligence of its attorneys in preparing the patent application and "constructive" reduction to practice, which was different from the theory of inventor diligence and actual reduction to practice it had argued before the PTO Board.

Motive to Collude

33. In opposing Genentech's priority argument in the Civil Action based on the Draft Cabilly Application, Celltech asserted that the draft fell short of satisfying the legal requirements for "conception" in that it did not set forth each and every element of the invention. Additionally, Celltech argued that Genentech had changed its basic theory of the case from what it asserted before the PTO Board, a tactic which is not permitted in appeals from PTO interference proceedings.

34. Genentech responded by pointing out that the Draft Cabilly Application contained at least as much detail as Celltech's March 25, 1983 British Patent Application. Separately, Genentech also moved for summary judgment that Celltech was not entitled to the March 25, 1983 priority date because of defects in the British Patent Application. Genentech's motion thus called into question whether Celltech had actually invented the disputed technology.

35. Thus, the dispute over the Draft Cabilly Application caused each party to argue that the other was not in possession of the "invention" at issue in early 1983. This new

posture meant that Genentech and Celltech each argued that the other was not entitled to the patent in question. Genentech and Celltech, which had waged this priority dispute for nine years, should have appreciated the possibility that at the end of a protracted legal battle, neither side would end up with a valid patent. This realization provided a strong motive for the Agreement that they entered.

36. The illegal and anticompetitive Agreement was reduced to writing by Genentech and Celltech sometime after July 31, 2000, when the Court denied Genentech's motions for summary judgment. Upon information and belief, Genentech and Celltech entered into the Agreement with a bad faith intent to limit and injure competition as illustrated by the fact that the Agreement called for Celltech to concede defeat to Genentech and sacrifice the Boss Patent. Celltech did so, notwithstanding the facts that it had just defeated Genentech's summary judgment motions based on the "newly discovered" evidence, and that Celltech had established priority in the PTO after a seven-year proceeding.

37. According to publicly available statements, the Agreement required Genentech to make Celltech whole by compensating Celltech for the royalties it would have received under the Boss Patent. Such "reverse payments" (so-called because they were made by Genentech, the nominal winner in the "settlement," to Celltech, the nominal loser) thus provided Celltech all the benefits it would have received had it preserved the victory it had earned at the PTO Board.

38. Indeed, the Agreement put Celltech in a position *better* than any outcome it could have obtained in litigation. Celltech has publicly admitted that Genentech agreed to give Celltech and its products "preferential access" to Genentech's New Cabilly Patent, which could keep competitors at bay, or at a competitive disadvantage, for *twelve years longer* than Celltech's Boss Patent could have done so.

## Genentech and Celltech Submit a Deficient Proposed Order to the District Court

39. The parties submitted a proposed order to the District Court in order to implement their Agreement. The proposed order contained a "finding" that Genentech won the priority controversy *as a matter of law* because the Draft Cabilly Application constituted evidence of "conception" prior to the Boss Patent. In fact, as Celltech had argued successfully in opposition to Genentech's summary judgment motion, the Draft Cabilly Application did no such thing in that it was missing certain key elements of the claimed invention. Having first convinced the Court that the Draft Cabilly Application did not prove conception as a matter of law, Celltech reversed course completely and asked the Court to find that it did.

40. Moreover, the findings in the proposed order were insufficient as a matter of law to declare Genentech the prevailing party. In addition to the requirement that Genentech show "conception" before the Boss priority date, it also was necessary as a matter of well established patent law for Genentech to show "reasonable diligence" during the critical period in order to pre-date the Boss Patent. Despite the fact that both Celltech and Genentech recognized and briefed this legal requirement in connection with the summary judgment motions, the proposed order contained no finding with respect to the essential requirement of "reasonable diligence." Moreover, Celltech's concession was flatly inconsistent with Celltech's previous argument that Genentech was precluded from relying on its proffered theory of "attorney diligence," having failed to raise this issue in the PTO interference proceeding.

41. Other than striking the word "proposed" in the title, the District Court on March 16, 2001 signed without change the proposed order that the parties had submitted jointly in

order to implement their illegal and anticompetitive Agreement (the "Order").

42. The March 16, 2001 Order (drafted by Genentech and Celltech) remanded the case back to the PTO Board for further action consistent with the Agreement. Specifically, the Order directed the PTO Board to do three things: (a) "to vacate the PTO's decision in *Cabilly, et al. v. Boss et al.*, Patent Interference No. 102,572"; (b) "to revoke and vacate United States Patent No. 4,816,397, issued March 28, 1989 to Boss, et al."; and (c) "to grant and issue to Genentech's Inventors (with Genentech as the assignee), *with the issue date being the same as the date of revocation of United States Patent No. 4,816,397* [the Boss Patent], a United States patent . . ." (Emphasis added).

PTO Board Expresses Concerns Regarding the Agreement

43. In response to the District Court's Order, the PTO Board revoked the Boss Patent, but refused to issue the New Cabilly Patent, noting that neither the parties nor the District Court had any authority to compel the PTO to issue a patent, particularly when the administrative examination process had not been completed.

44. The fact that the Agreement called for the instantaneous issuance of the New Cabilly Patent, when the parties well knew that the examination process had not been completed, is further evidence of their bad faith and their intent to prevent the PTO from examining the patentability of the alleged invention.

45. The PTO Board expressed concerns about the parties' Agreement. Among other things, the PTO Board noted that the Agreement effectively created a 29-year patent: "We will note that if a patent is issued to Cabilly, its term will begin to run now and the public has already been subject to patent rights of Boss since 1989, and that the interference has been pending since 1991."

46. Additionally, the PTO Board expressed concern that Celltech had seemingly abandoned a winning position. In particular, there was no indication that Celltech had raised with the District Court the issue of whether Genentech's "newly discovered" Draft Cabilly Application should have been precluded from evidence because Genentech had not shown that it was diligent in locating this evidence during the more than seven year interference proceeding before the PTO Board.

47. In response to the PTO's refusal to issue the New Cabilly Patent to Genentech at the same time it revoked the Boss Patent, *Celltech* filed a new federal court action in the United States District Court for the Northern District of California seeking an order directing the PTO to issue a patent to Genentech. Thus, it appears that Celltech claimed to be aggrieved by the failure of the PTO to issue a patent to *Genentech*. Because of the Agreement, however, Celltech's concern was understandable: Not only had Genentech agreed to make Celltech whole for any "lost" royalties from the Boss Patent, but Genentech had also agreed to give Celltech "preferential access" to its New Cabilly Patent; thus, it was now in Celltech's interest to have the New Cabilly Patent issue so that it could jointly dominate the market with Genentech.

Examination of the New Cabilly Application:

Inequitable Conduct

48. Despite its stated reservations, the PTO Board referred the New Cabilly Application to a patent examiner to continue prosecution, given that a major impediment to the issuance of the patent (namely, the Boss Patent) had now been removed by the agreement between Genentech and Celltech resolving the priority dispute.

49. Given that the PTO had issued identical claims in 1989 in the form of the Boss Patent, the PTO had no reason to

believe that the claims that Genentech sought in the New Cabilly Application were unpatentable, nor was the PTO given any reason to consider this issue while the interference was still pending. Indeed, the only direction that the PTO Board gave to the PTO examiner was to consider certain references that Genentech had submitted in 1991, *after* the PTO had declared the interference. There is no indication that the PTO examiner handling the matter in 1991 ever considered these references.

50. Thus, after the July 25, 2001 PTO Board decision, prosecution of the New Cabilly Application resumed before a new patent examiner who had no familiarity with the previous prosecution of this application, much less with the interference proceeding in the PTO or the resulting Civil Action.

51. During examination of the New Cabilly Application, while under a duty of candor to the PTO, Genentech and/or COH engaged in inequitable conduct with intent to mislead to PTO in an effort to obtain the New Cabilly Patent.

Patentability Defects

52. Genentech failed to comply with its duty of candor to the PTO because it failed to provide to the PTO examiner meaningful disclosure of the significant, material issues as to the patentability of the claimed invention which became known to Genentech no later than during the course of the summary judgment briefing in the Civil Action.

53. During the course of the Civil Action, Celltech developed and presented expert evidence that cast serious doubt upon whether Genentech's final (or draft) New Cabilly Application enabled the claimed invention, which is a requirement of section 112 of the patent laws. Celltech's expert opined that "Genentech's purported 'conception' lacked a critical component: the Genentech inventors never came up with a workable method for producing 'an Ig [immuno-

globulin] molecule or an immunologically functional Ig fragment' as the [interference] Count requires. Celltech has presented expert testimony . . . showing that Genentech's [final] patent application and laboratory notebooks are completely devoid of a workable conception because of this failing. In particular, Genentech lacked a method for combining ('refolding') the recombinantly expressed heavy and light chain proteins into a functional molecule." Opposition to Genentech's Motion for Summary Adjudication that Genentech Conceived of the Invention Before March 25, 1983 at p. 1. In other words, Celltech offered evidence that Genentech's final New Cabilly Application did not enable the disputed invention as required by 35 U.S.C. § 112.

54. Additionally, Celltech's expert Dr. Jonathan S. Weissman concluded in his expert report (which was quoted in Celltech's Opposition to Genentech's Motion for Summary Adjudication that Genentech Conceived of the Invention Before March 25, 1983) that "Expression of the heavy and light chains from transformed *E. coli* host cells as described in Genentech's patent application does not produce correctly folded Ig molecules or immunogologically functional Ig fragments. . . . [A]s of March 25, 1983, a scientist of ordinary skill in the art would not, without extensive experimentation, have been able to arrive at refolding conditions capable of generating an immunologically functional protein. Indeed, even after extensive experimentation, proper folding conditions may not have been possible to find. Genentech never determined such refolding conditions."

55. *A fortiori*, if Genentech's final New Cabilly Application was insufficient evidence of a complete conception because it lacked a solution to the refolding problem, as Celltech urged, then the Draft Cabilly Application, which was the basis for the settlement, was also insufficient. Indeed, the Draft Cabilly Application had a section heading entitled "Reconstitution [refolding] of Antibody from Recombinant *k*

and Gamma Chains." However, that section of the Draft Cabilly Application was completely blank. Therefore, the Draft Cabilly Application (which formed the basis of Genentech's priority claims in the Civil Action) had absolutely no teaching on a critical part of the purported invention.

56. Thus, no later than the summary judgment briefing, Genentech became aware of evidence raising issues as to the patentability of the New Cabilly Application claims because of a lack of enablement. Such information was material because it would be important for a reasonable PTO examiner to consider any evidence that called into question the patentability of claims sought in prosecution.

57. Genentech responded to Celltech's evidence by asserting that its newly discovered Draft Cabilly Application contained the "same" detail as Celltech's March 25, 1983 British Patent Application, which was the basis for Celltech's claim of priority. Genentech reasoned that if Celltech's 1983 British Patent Application was sufficient to demonstrate enablement of the disputed invention (as Celltech had implicitly argued to the PTO), then the Draft Cabilly Application also must be sufficient because, according to Genentech, it "contains the same information." Genentech's Motion for Summary Adjudication that Genentech Conceived of the Invention Before March 25, 1983.

58. However, at the same time Genentech answered Celltech's attack on the legal sufficiency of the Draft Cabilly Application by *equating* it to Celltech's British Patent Application, Genentech launched its own assault on the legal sufficiency of the very same British Patent Application.

59. Specifically, during Genentech's deposition of Celltech's Expert, Dr. Weissman at pp. 135-36, Genentech asked "[d]o you have any opinion as to whether [Celltech's British Patent Application] would have been sufficient to teach one of ordinary skill how to reassemble the light and heavy chains

*as* of March 25, 1983," to which Dr. Weissman answered "[i]t's not sufficient."

60. Accordingly, Genentech asserted, "Celltech's British Application was 'not sufficient' to teach one of ordinary skill how to make and use the invention, because . . . the '[f]olding of an immunoglobulin is a difficult problem.' . . As a matter of law, Celltech is not entitled to a priority date based on its [March] 25, 1983 British application." Motion for Summary Adjudication that Celltech is Not Entitled to a Priority Date Based on its British Patent Application.

61. Thus Genentech found itself in the position of arguing (1) that "its February 25, 1983 application contains the *same information* . . as Celltech's British Patent priority document . . . ." Reply Brief Supporting its Motion for Summary Adjudication that Genentech Conceived of the Invention Described by the Court before March 25, 1983, and (2) that Celltech's British Patent Application did not enable the invention in accordance with 35 U.S.C. § 112.

62. The logical conclusion of these two arguments, which *Genentech* made simultaneously, was that Genentech's Draft Cabilly Application was not enabling because it was not sufficient to teach one of ordinary skill how to make and use the invention, specifically with respect to the issue of teaching the "folding" of irnmunoglobulins. .Genentech asserted that Celltech's disclosure was deficient in thus regard, yet in the extensive summary judgment briefing in the Civil Action, Genentech noted that its own disclosure had the "same information" as that of Celltech. Genentech never identified any disclosure relating to refolding in its Draft Cabilly Application (or, indeed in its final application) that provided what Genentech asserted was lacking in Celltech's British Patent Application.

63. Genentech's arguments in the summary judgment briefing (*i.e.* equating the disclosure of its Draft Cabilly Application with that in Celltech's British Patent Application

while simultaneously attacking the sufficiency of that same disclosure) both undercut its position that the Draft Cabilly Application entitled Genentech to priority of invention and demonstrated that Genentech believed that it was essential to have enabling disclosure of refolding in its final New Cabilly Application. Thus, by its own admissions, the issue of refolding was material to the patentability of the claims of the New Cabilly Application.

64. Moreover, the fact that each of Celltech and Genentech was attacking the adequacy of the other application suggested that neither Genentech nor Celltech had properly enabled the invention over which they had fought for nearly ten years. Genentech did not direct the PTO examiner to the fact that Celltech's expert was of the view that neither Genentech nor Celltech had solved the problem of antibody refolding in 1983, the time of the alleged invention.

65. These attacks put the parties on a collision course that could have resulted in neither party emerging from the Civil Action with a valid patent. At the very least, a lengthy public trial developing a detailed factual record concerning these issues would have provided a roadmap for any third party to invalidate whichever patent emerged from the squabble.

66. This collision course gave the parties the motive to enter into a collusive settlement agreement to preserve the patent by agreement. One of the terms of the settlement was that the PTO issue the New Cabilly Patent immediately, and thus without further examination. The PTO Board noted that this was improper. However, the parties' attempt to circumvent the examination process is compelling evidence of the parties' bad faith intent to ensure that there would be no opportunity for the PTO to consider whether the claims were patentable.

67. Once it became aware of the defects in the enablement of the invention, and particularly once patent prosecution resumed before a new examiner after the order of the PTO

Board following the settlement, Genentech had an obligation to reveal the serious questions regarding the patentability of the claimed invention that had come to light during the Civil Action, including a duty to direct the examiner to the expert testimony of Celltech's expert Dr. Jonathan S. Weissman and the admissions that Genentech had itself made (described above) regarding the inadequacy of Genentech's own invention disclosure.

68. Genentech never directed the PTO to these new enablement issues that arose from Celltech's evidence concerning refolding, and from Genentech's own statements, notwithstanding its awareness of the problem and notwithstanding that this would have been material to the examiner in determining whether to issue the patent.

69. This is particularly egregious given that after the New Cabilly Application was sent back for continued examination, as a matter of patent practice and procedure, the new PTO examiner would not *sua sponte* have raised new issues regarding the patentability of the claimed invention under 35 U.S.C. § 112.

70. Therefore, Genentech had a duty to raise the patentability issues to the PTO examiner that had not been previously disclosed to the prior PTO examiner.

71. Indeed, there is no evidence that these issues relating to refolding ever occurred to the new PTO examiner who was charged with assessing the New Cabilly Application in the context of ex parte patent prosecution. Moreover, it was particularly unlikely that the PTO examiner would on his own seek out new issues relating to patentability given the posture of this examination, *i.e.*, the examiner was faced with an order (drafted by Genentech and Celltech) from a United States District Court purporting to direct the PTO to issue a patent to Genentech forthwith and an additional order from the PTO board identifying only the materials submitted in

1991 as a barrier standing in the way of issuance of a patent to Genentech.

72. Under these circumstances, which Genentech orchestrated, Genentech had a duty to advise the examiner of any new issues relating to patentability that had arisen during the decade-long priority dispute.

73. Moreover, because Genentech had equated the disclosure in the Draft Cabilly Application and that in Celltech's British Patent Application, it also should have alerted the PTO examiner to evidence—which Genentech elicited and upon which Genentech relied in the Civil Action—that Celltech's refolding expert believed that Celltech's British Patent Application was deficient. By Genentech's own admission, this was evidence that the Draft Cabilly Application—which Genentech represented contains the *"same information"*—was similarly flawed, thus undercutting the basis for Genentech's priority claim.

74. Having challenged the adequacy of Celltech's disclosure (during the Civil Action) with respect to immunoglobulin refolding, Genentech knew that this refolding issue would have been material to the examiner. Still, Genentech never raised this issue with the examiner.

75. Genentech may claim that it discharged its duty of candor to the PTO by providing the pleadings pertaining to the Civil Action to the PTO and may assert further that the PTO "considered each reference." However, Genentech's dumping of some eleven bankers boxes of pleadings, deposition transcripts, exhibits, affidavits, expert reports and other materials on the PTO *the same day* that the examiner advised Genentech in an interview that he would allow the claims to issue, and just *one day before* the examiner issued the Notice of Allowability of the patent did not satisfy Genentech's duty of candor to the PTO. Genentech never advised the examiner of the significant potential flaws in patentability that had been exposed during the Civil Action.

76. Genentech, well aware of the circumstances of the collusive settlement, attempted to sneak the damaging Civil Action materials into the PTO under circumstances that virtually guaranteed that the examiner would be unable to give them any serious consideration. Genentech made no effort to direct the examiner's attention to any particular materials in the approximately eleven bankers boxes dumped on the PTO at the last minute.

77. Upon information and belief, Genentech submitted the voluminous materials from the Civil Action without saying a word about their contents with intent to deceive and for the express purpose of being able to argue in future patent litigation that the PTO had considered all that occurred in the Civil Action, but nonetheless gave the New Cabilly Patent its approval.

78. Genentech's inequitable conduct, however, did not end with its failure to reveal to the examiner serious non-enablement problems relating to the "refolding" aspect of the claimed invention. Genentech was also responsible for other egregious conduct, including failing to disclose contradictory positions Genentech had taken regarding the significance of material prior art, deluging the examiner with hundreds of prior art references without directing the examiner to those that were most material, and also failing to disclose certain prior art at all, despite having knowledge of such art.

Failure to Disclose Contradictory Positions
On The Vallé Prior Art

79. Genentech failed to disclose to the PTO the fact that it had taken a position about a material prior art reference that contradicted the position that Genentech was taking before the examiner in order to attempt to obtain issuance of the New Cabilly Patent.

80. After declaration of the interference, Genentech submitted a number of references to the PTO examiner in an

Information Disclosure Statement dated September 18, 1991. Genentech cited a number of prior art references disclosing the generation of recombinant immunoglobulin molecules using cells known *as* "oocytes." One of these references was Vallé *et al., Anti-ovalbumin monoclonal antibodies interact with their antigen in internal membranes of Xenopus oocytes,* 300 Nature 71 (1982)("Vallé").

81. In its 1991 filing, Genentech represented that the Vallé article was not invalidating prior art because "[w]ork of this sort is *readily distinguishable* from the instant claims in that the oocytes are not transformed with DNA, but instead are used to transiently express mRNA preparations." (emphasis added).

82. Several years after the submission of Vallé to the PTO, and its representation that Vallé was "readily distinguishable," Genentech made completely inconsistent statements, in another forum, about the significance of this reference. At the same time that Genentech was waging a decade-long priority dispute with Celltech over rights to the invention claimed by the U.S. Boss Patent, Genentech was mounting a separate attack on the validity of the European version of Celltech's Boss Patent (the "European Boss Patent"), which contained the identical specification to Celltech's U.S. Boss Patent and virtually identical claims to the U.S. Boss Patent. Thus, the European Boss Patent claims that Genentech attacked were nearly identical to the claims of the New Cabilly Patent that issued to Genentech in December 2001.

83. In an April 19, 1994 Notice of Opposition proceeding (EP-B-0120694 (84301996.9)) before the European Patent Office ("EPO"), Genentech opposed Celltech's assertion that it was entitled to these patent claims. Genentech submitted a document to the EPO which attacked the validity of these claims based on the same Vallé "oocyte" reference it had distinguished before the U.S. PTO.

84. More particularly, Genentech asserted in Europe that Vallé was material prior art. In the process, Genentech trivialized the distinction between mRNA (messenger RNA), which was used in the Vallé article, and DNA, which was claimed in the European Boss Patent application: "[i]n view of the broad implications evidenced by the Abstract, the fact that the actual experiment was performed with microinjected mRNAs is not relevant. In any event, because the messenger RNA carries the information from DNA to the ribosomal site of protein synthesis, it is *functionally equivalent* to DNA." (emphasis added).

85. This representation was diametrically opposed to Genentech's statements to the PTO. When comparing the same prior art reference against the same claimed subject matter, what was "readily distinguishable" before the PTO became "functionally equivalent" before the EPO.

86. As of April, 1994, while the New Cabilly Application was still pending, (on or in any event no later than July 25, 2001, when the PTO Board directed the PTO to examine the New Cabilly Patent Application), Genentech had a duty to advise the PTO examiner that it had arrived at the conclusion that the use of messenger RNA in Vallé was "functionally equivalent to DNA." Not only would this insight have been material to a reasonable examiner in its own right, but its materiality was enhanced by the fact that Genentech's new position contradicted its representation to the PTO in September 1991 that the Vallé work was "readily distinguishable" because it involved messenger RNA rather than DNA.

87. In its July 25, 2001 order, the PTO Board singled out the 1991 Information Disclosure Statement, which contained Genentech's now contradicted statements about the Vallé reference, for consideration by the examiner when prosecution resumed. Thus, Genentech's 1991 statements were being presented in 2001 to a new examiner responsible for considering the New Cabilly Application. These developments

only heightened Genentech's existing obligation to provide complete disclosure with respect to the material Vallé reference, including disclosure of its 1994 conclusions about this reference and its inconsistent statements about the same reference while opposing Celltech's efforts to obtain nearly identical claims in Europe.

88. Despite its obligation to do so, Genentech never advised the PTO examiner of its 1994 conclusions with respect to the Vallé reference, its EPO statements in that regard, and the fact that its EPO statements directly contradicted what it had told the PTO years earlier. When the PTO Board directed the examiner to consider, in 2001, the Information Disclosure Statement Genentech filed in 1991, Genentech was effectively reaffirming its 1991 representation to the PTO, which it had plainly abandoned no later than 1994.

89. It would have been important for a reasonable examiner to know all these facts about the Vallé reference, which disclosed a recombinant antibody. Genentech itself plainly believed the reference was material to the claimed invention, as demonstrated by Genentech's reliance upon the Vallé reference as the centerpiece of its attack upon the validity of the European Boss claims, which were virtually identical to the claims Genentech was seeking.

90. Because Genentech made affirmative statements to the PTO about this reference in 1991, it was materially misleading for Genentech to fail to tell the PTO about its 1994 positions and its contradictory statements to another patent office about these same references.

91. Based on the protracted high profile legal battle between Genentech and Celltech both in the U.S. and Europe, Genentech's treatment of the Vallé reference in the U.S. (making special efforts to distinguish it) and Europe (basing an invalidity case upon it), Genentech's high level of sophistication, and the extraordinary measures that Genentech

took over many years to secure allowance of the New Cabilly Patent, it is evident that Genentech withheld its contradictory statements about the Vallé reference with an intent to deceive the PTO.

Burying Prior Art

92. Genentech also committed inequitable conduct by deluging the examiner with more than *350* prior art references, in addition to the eleven banker boxes containing the documents related to the Civil Action. Strikingly, in the Information Disclosure Statement dated September 13, 2001 alone, Genentech dumped more than *275* references on the examiner.

93. To put this conduct into perspective, in the thirteen years that passed between Genentech's filing of the New Cabilly Application in 1988 through September 12, 2001, Genentech advised the PTO of approximately 75 prior art references. Then in the last few weeks of prosecution, Genentech submitted more than *275* additional references.

94. Since Genentech submitted such a large number of references, under its duty of candor generally and under the principles summarized in section 2400(13) of the Manual of Patent Examining Procedure, it should have "highlight[ed] those documents which have been specifically brought to the applicants attention and/or are known to be of most significance." Genentech never did this.

95. Moreover, if Genentech had any genuine interest in providing meaningful disclosure to the PTO, it could have begun the disclosure process long before it did so. Genentech understood that the pendency of the interference was no bar to the submission of prior art references, as demonstrated by Genentech's submission of the Vallé reference and other articles concerning oocytes after declaration of the interference. Genentech also could have submitted these references once it got the District Court to sign the jointly

proposed March 16, 2001 order directing the PTO to issue the New Cabilly Patent. The reason Genentech waited until the last minute to disclose these prior art references was, as demonstrated by the March 16, 2001 order drafted by it and Celltech, that Genetech intended to orchestrate the settlement so as to avoid any further examination of the New Cabilly Patent.

96. The dumping of these voluminous and dense prior art references in a single Information Disclosure Statement—just a few weeks before the notice of allowability of the patent was issued on October 5, 2001—and without directing the examiner to those of the greatest significance had the effect of "burying" a material piece of prior art: Stanford University's European Patent Application, EPO No. 0,044,722 (the "Stanford Application").

97. The Stanford Application is a material reference because it teaches the production of recombinant antibodies in bacterial host cells by use of *DNA* encoding the heavy and light chains of an antibody. The Stanford Application teaches a procedure essentially identical to the procedure disclosed in the New Cabilly Application and which formed the basis for the claims in the New Cabilly Patent.

98. It would have been important to a reasonable examiner for Genentech to highlight the significance of the Stanford Application, particularly given Genentech's position before the PTO that Vallé was "readily distinguishable" because it used mRNA instead of DNA. In contrast, the Stanford Application teaches use of DNA, as is claimed in the New Cabilly Patent. Instead, Genentech made no effort to highlight this reference in any way as compared to the approximately 275 other references submitted on the same day.

99. Based on the surrounding circumstances, including the materiality of the Stanford Application, the volume of the references submitted, the timing of such submissions and

Genentech's attempts to avoid any examination of the New Cabilly Application, Genentech buried the Stanford Application with an intent to deceive the PTO.

Failure to Disclose Material Prior Art

100. Genentech also committed inequitable conduct by failing to disclose anywhere among the more than *350* total references critical prior art references that fully anticipate or, in combination with other references, render obvious the claims of the New Cabilly Patent: U.S. Patent No. 4,399,216 (the "'216 Patent"), U.S. Patent No. 4,634,665 (the "'665 Patent") and U.S. Patent No. 5,179,017 (the "'017 Patent") (collectively the "Axel Patents").

101. The Axel Patents are material references because they all disclose a process for inserting DNA into cells to produce proteinaceous materials, and at least the first such patent (the '216 Patent) expressly claimed generation of a recombinant antibody molecule through the transformation of a cell with *DNA*. Thus, Genentech would not have been able to distinguish this reference on the grounds used to distinguish the Vallé reference.

102. Genentech knew of the existence and significance of the '216 Patent and '665 Patent during the prosecution of the New Cabilly Patent because, *inter alia*, it has alleged that it paid some seventy million dollars in royalties on account of those patents (presumably for its recombinant antibody products) for the years 1987 through 2000, according to a complaint that Genentech filed against Columbia University. *See Genentech, Inc. v. The Trustees of Columbia University of the City of New York*, Civ. No. 03-1603 (N.D. Cal. 2003).

103. Upon information and belief, Genentech also knew of the existence of the '017 Patent during prosecution of the New Cabilly Application based on the significant royalties it was paying on its predecessor patents (the '216 Patent and the '665 Patent), and because Genentech alleges that it had a

license with Columbia for "certain" other "patent applications" involving the Axel disclosure.

104. Despite its knowledge of the Axel Patents during the prosecution of the New Cabilly Patent, Genentech never brought the Axel Patents to the examiner's attention.

105. Disclosure of the Axel Patents would have been important to a reasonable examiner in considering the patentability of the New Cabilly Patent claims, given that they all disclose a process for inserting DNA into cells to produce proteinaceous materials, and that the '216 Patent specifically claimed recombinant production of an antibody by use of DNA, the same subject matter claimed in the New Cabilly Patent.

106. Upon information and belief, based on the circumstances surrounding Genentech's omission of the Axel Patents as references, including their materiality for the reasons stated above, Genentech's awareness of these patents and their significance in the recombinant antibody field based on Genentech's large royalty payments to Columbia University, and based on the lengths to which Genentech was willing to go to obtain issuance of the New Cabilly Patent, including entering a collusive settlement agreement that went so far as to command the PTO to issue the New Cabilly Patent without further examination, Genentech omitted the Axel Patents as a prior art references with the intent to deceive the PTO in order to obtain issuance of the New Cabilly Patent.

Issuance of the New Cabilly Patent

107. Subsequent to Genentech's misrepresentations and material omissions to the PTO, the New Cabilly Patent, U.S. Patent No. 6,331,415B1, issued on December 18, 2001.

108. The New Cabilly Patent is titled "Methods of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein." It lists as inventors Shmuel Cabilly,

Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs and Ronald B. Wetzel and Genentech as the assignee. A Certificate of Correction issued by the PTO on June 25, 2002 added COH as an additional assignee.

109. The New Cabilly Patent purports to cover "processes for producing an immunoglobulin or an immunologically functional immunoglobulin fragment . . . in a single [host] cell" and, according to Genentech's press release, purportedly relates to the "fundamental methods and compositions used to produce antibodies by recombinant DNA technology." When injected into humans, these antibody molecules (sometimes referred to as "immunoglobulins") can help prevent disease.

110. On the same day the New Cabilly Patent was issued, Celltech issued a press release revealing some of the terms of its illegal and anticompetitive Agreement with Genentech. Celltech admitted that "Celltech will be compensated by Genentech in terms of income from sales of products which would have been covered by the Boss Patent until its normal expiring date in 2006." Thus, notwithstanding the fact that the Boss patent was revoked by the PTO Board in 2000 (pursuant to the Agreement of the parties), upon information and belief, Celltech effectively continues to receive royalties until 2006. Receipt of royalties after patent expiration constitutes *per se* patent misuse.

111. Moreover, the Celltech press release notes that Celltech is to receive favored treatment under the New Cabilly Patent. The release says that "Celltech also . . . secured preferential access for its development programes to the Cabilly patent, which covers the production of a broad range of antibody or antibody fragment products, for its 17 year life." However, the parties have not disclosed the precise terms of this "preferential access."

Secrecy and Potentially Improper Filing of Agreement with the PTO

112. Pursuant to 35 U.S.C. § 135(c), any agreement to settle a patent interference proceeding must be filed with the PTO. As the Senate Report related to this legislation explains, "[i]nterference proceedings may be terminated in a manner hostile to the public interest by using patent interference settlement agreements as a means of restricting competition. To make such a practice more difficult the bill requires the filing of such agreements in the Patent Office." Defendants have filed the document under seal, preventing MedImmune and the public from determining the exact terms of the Agreement or even if it was filed within the prescribed time limits. A failure to file an agreement terminating an interference within the prescribed limits will result in a finding that the patent is permanently unenforceable.

113. In a letter dated February 13, 2002, MedImmune requested a copy of the Agreement from Genentech.

114. Genentech denied MedImmune's request for a copy of the Agreement in a letter dated March 24, 2002, stating that "the settlement agreement is a confidential document, and we cannot provide it to you."

115. On May 8, 2002, MedImmune petitioned the PTO for access to this Agreement, and on July 22, 2002, continuing in their efforts to conceal the Agreement from public scrutiny, both Celltech and Genentech opposed MedImmune's petition. The PTO denied MedImmune's request for access to the Agreement.

*GENENTECH REAPS THE BENEFIT OF THE NEW CABILLY PATENT MONOPOLY*

116. In public statements Genentech has taken the position that the New Cabilly Patent is extremely broad. For example, Genentech's vice president of intellectual property, Sean

Johnston, has stated "we do not believe that the claims are limited by type of antibody (murine, humanized [90% human sequence] or human) or by host cell type" and that "the recently issued patent broadly covers the co-expression of immunoglobulin heavy and light chain genes in a single host cell." In other words, Genentech asserts that the New Cabilly Patent broadly covers the basic method of artificially producing any monoclonal antibody using recombinant DNA technology in any type of host cell.

117. Consistent with this position, in a letter dated January 7, 2002, Genentech advised MedImmune of its "expectation that MedImmune will pay royalties on sales of its Synagis® antibody product pursuant to the license granted by Genentech under the recently issued U.S. Patent No. 6,331,415 [the New Cabilly Patent]."

118. In a letter dated February 13, 2002, MedImmune disputed this demand for royalty payment and requested an explanation of Genentech's "basis for believing that MedImmune's product would infringe any valid claim of the [New Cabilly] Patent such that royalties would be due" and also requested a copy of the Agreement.

119. Receiving no response to its February 13, 2002 letter and fearing the commencement of patent infringement litigation by Genentech before MedImmune could complete its investigation as to the validity and/or enforceability of the New Cabilly Patent, MedImmune made the requested royalty payment, but in a letter dated March 8, 2002 stated that "[s]uch payment, however, was made under protest and with reservation of all of our rights." MedImmune continues to make such royalty payments on a quarterly basis.

*INJURY TO MEDIMMUNE AND COMPETITION*

120. The Agreement substantially and adversely affects MedImmune in particular and competition in the biotechnology industry in general by limiting access to what Genen-

tech now claims is the core technology for the production of artificially synthesized antibodies.

121. Prior to the Agreement, Celltech controlled this technology through its interest in the Boss Patent, and had authorized the Medical Research Council in London ("MRC") to grant sublicenses to the Boss Patent, which it did liberally and with minimal field of use restrictions.

122. Upon information and belief, MedImmune was one of many biotechnology companies that obtained a sublicense to the Boss Patent at a previously established royalty rate.

123. However, the Agreement effectively nullified the sublicenses freely granted by MRC to technology that would lose patent protection in 2006, and now leaves companies at the mercy of Genentech to acquire new licenses to the New Cabilly Patent, a patent which will not expire until 2018.

124. Genentech is in a position to use the New Cabilly Patent to force biotechnology companies, including MedImmune, to pay substantial royalties to retain access to the same technology that Celltech (through MRC) had once licensed to them, or simply be denied access altogether.

125. The New Cabilly Patent has damaged MedImmune in the form of the payments to Genentech under the 1997 License Agreement based on sales of Synagis®. (In addition to payments to Genentech on account of the New Cabilly Patent, MedImmune continues to pay royalties to MRC despite revocation of the Boss Patent because the Boss Patent license was part of a package with another patent.) Additionally, MedImmune has, as a practical matter, been compelled—at great cost—to enter into the 2003 License Agreements with Genentech to protect its investments in seven critically important products in various stages of preclinical and clinical trials, including the antibodies Vitaxin and Medi-507, and antibodies against each of EphA2, IL-9, PC-Cell-Derived Growth Factor ("PCDGF"), Human

Aspartyl (Asparaginyl) BetaHydroxylase ("HAAH"), and Human Metapneumovirus ("hMPV"), which target, among other illnesses, cancer, asthma and other respiratory diseases, rheumatoid arthritis and psoriasis. These substantial payment obligations to Genentech under the License Agreements, on account of the New Cabilly Patent, harm MedImmune's ability to compete in its sale of antibody products.

Relevant Market

126. The relevant market is the fundamental recombinant DNA technology for producing antibodies, including the process for producing an immunoglobulin or an immunologically functional immunoglobulin fragment in a single host cell that is purportedly covered by the claims of the New Cabilly Patent.

127. This technology, as interpreted by Genentech, is an essential component to the commercial manufacture of monoclonal antibodies. Upon information and belief, there is no known commercially viable method for recombinantly producing therapeutic antibody molecules without this technology, assuming that the New Cabilly Patent is as broad as Genentech says it is. If so, upon information and belief, no known proven alternative to this technology exists currently, and the development of any such alternative would require substantial investment of money, resources and time, and cannot reasonably be expected in the foreseeable future.

128. The relevant geographic market is the entire United States.

Market Effects

129. The unlawful conduct of Genentech and Celltech has required MedImmune and, upon information and belief, other users of this technology to obtain new licenses and/or pay additional and substantial royalties under extant licenses for a term beyond that contemplated under existing patent law, or to be excluded from use of this technology.

130. The unlawful conduct of Genentech and Celltech and the resulting issuance of the New Cabilly Patent has diminished the incentive of MedImmune and other users of the technology to invest in products making use of the technology.

*FIRST CAUSE OF ACTION:*

*DECLARATORY JUDGMENT ON CONTRACTUAL RIGHTS AND OBLIGATIONS*

(Against Genentech)

131. MedImmune incorporates the allegations of paragraphs 1 through 130 as if fully set forth herein.

132. An actual controversy has arisen and now exists between the parties concerning the rights and obligations of MedImmune under the terms of the License Agreements. Genentech has demanded that MedImmune make payments under the 1997 License Agreement on the basis that Synagis® would infringe a valid claim of the New Cabilly Patent but for the 1997 License Agreement. MedImmune disputes its obligation to make payments under the 1997 License Agreement because MedImmune's sale of its Synagis® product does not infringe any valid claim of the New Cabilly Patent. The basis for invalidity of the New Cabilly Patent arises under the patent laws of the United States, 35 U.S.C. §§ 101, 102, 103, 112, *et seq.* and/or the judicially created doctrine of obviousness type double patenting.

133. MedImmune hereby seeks a declaratory judgment that it owes no payments under the License Agreements.

*SECOND CAUSE OF ACTION:*

*PATENT INVALIDITY*

(Against Genentech and COH)

134. MedImmune incorporates the allegations of paragraphs 1 through 133 as if fully set forth herein.

135. An actual controversy has arisen and now exists between the parties concerning the validity of the New Cabilly Patent.

136. The New Cabilly Patent is invalid because it is anticipated and/or obvious under 35 U.S.C. §§ 102 and/or 103.

137. The New Cabilly Patent is invalid based on the judicially created doctrine of obviousness type double patenting and/or under 35 U.S.C. §§ 101 and/or 103.

138. The New Cabilly Patent is invalid under 35 U.S.C. § 112.

139. MedImmune hereby seeks a declaratory judgment that the New Cabilly Patent is invalid under 35 U.S.C. §§ 101, 102, 103, 112, *et seq.* and/or under the judicially created doctrine of obviousness type double patenting:

*THIRD CAUSE OF ACTION:*

*PATENT UNENFORCEABILITY*

(Against Genentech and COH)

140. MedImmune incorporates the allegations of paragraphs 1 through 139 as if fully set forth herein.

141. An actual controversy has arisen and now exists between the parties concerning the enforceability of the New Cabilly Patent.

142. Based on the status of Genentech and COH as assignees of the New Cabilly Application and the resulting New Cabilly Patent, Genentech and COH controlled and/or had knowledge of the prosecution of the New Cabilly Application and are both accountable for the material misstatements and omissions made with intent to deceive the PTO. Neither assignee may enforce the New Cabilly Patent if there was inequitable conduct during prosecution.

143. During examination of the New Cabilly Application before a new examiner, while under a duty of candor to the PTO, Genentech and/or COH engaged in inequitable conduct with intent to mislead to PTO in an effort to obtain the New Cabilly Patent.

144. As explained in greater detail above, specifically at paragraphs 48 through 106, the duty of candor was not satisfied by Genentech and/or COH during the examination of the New Cabilly Application.

145. As explained in paragraphs 52 through 78, Genentech and/or COH failed to direct the PTO examiner to potentially significant flaws in the patentability of the claimed invention (*i.e.*, relating to non-enablement) which at least Genentech became aware of no later than during the course of the Civil Action.

146. In particular, Celltech attacked the adequacy of the New Cabilly Application with respect to its teachings relating to antibody "refolding." Genentech, in turn, attacked Celltech's specification as deficient in this respect and then, oddly, asserted that Genenetch's Draft Cabilly Application had the "same information" as that of Celltech's priority document. In short, by Genentech's own admission, its Draft Cabilly Application lacked enabling disclosure of the claimed invention, and Genentech never pointed to any disclosure in its final specification that cured this problem.

147. Genentech and/or COH never directed the PTO to Celltech's attacks on the adequacy of the New Cabilly Application or to Genentech's admissions about the deficiency of its own disclosure.

148. Based on the circumstances described in paragraphs 52-78, and as alleged in paragraphs 66 and 76-77, Genentech and/or COH failed to direct the PTO to these issues that raised doubt as to the patentability of the claims that issued as the New Cabilly Patent with an intent to deceive the PTO.

149. Second, as explained in paragraphs 79 through 91, Genentech and/or COH failed to advise the PTO examiner of Genentech's conclusion that the Vallé prior art reference, involving mRNA, was "functionally equivalent" to the invention claimed by the New Cabilly Patent which expressly claims "DNA," and the fact that Genentech had made a statement in the EPO in 1994 to that effect, contradicting its 1991 position before the PTO.

150. Based on the circumstances described in paragraphs 79-91, and as alleged in paragraph 91, Genentech and/or COH failed to disclose Genentech's contradictory conclusion and statement about the Vallé reference with an intent to deceive to PTO.

151. Third, as explained in paragraphs 92 through 99, Genentech and/or COH "buried" a material prior art reference, the Stanford Application, among more than *275* other dense prior art references, preventing meaningful review of the reference by the examiner.

152. Based on the circumstances described in paragraphs 92-99, and as alleged in paragraphs 95 and 99, Genentech and/or COH buried the Stanford Application with an intent to deceive the PTO.

153. Fourth, as explained in paragraphs 100 through 106, Genentech and/or COH failed to disclose—at all—material pieces of prior art, the Axel Patents.

154. Based on the circumstances described in paragraphs 100-106, and as alleged in paragraph 106, Genentech and/or COH omitted the Axel Patents as references with an intent to deceive the PTO.

155. These incidents of inequitable conduct are all thematically related. Aware of potential patentability flaws exposed no later than the time of the summary judgment briefing in the Civil Action, Genentech orchestrated the

agreement to avoid any PTO examination whatsoever. When the PTO rebuffed that attempt, Genentech turned to misrepresentations and non-disclosures as tools to obtain its patent.

156. As evidenced by the position it took on Vallé before the EPO in 1994, Genentech was well aware that prior work by others involving mRNA could very well make Genentech's DNA claims unpatentable, given that mRNA and DNA are, to use Genentech's words in Europe, "functionally equivalent." Notwithstanding its awareness, Genentech never disclosed its 1994 position to the PTO, leaving the PTO instead with the impression Genentech created in 1991 that the Vallé article was "readily distinguishable" from the claimed invention because it involved mRNA, not DNA.

157. This attempt to downplay Vallé in the PTO makes the burying of the Stanford Application all the more improper—as the Stanford Application teaches the use of DNA.

158. The complete failure to cite the Axel Patents, despite at least Genentech's knowledge of them and payment of royalties on at least two of them, was insidious as well because at least the '216 Patent claimed DNA, not mRNA in the making of an antibody.

159. Thus, on information and belief, Genentech very well knew that it could not distinguish these material pieces of prior art on the same basis it had "distinguished" Vallé—thus it buried one of them and failed to disclose the Axel Patents altogether.

160. The New Cabilly Patent is unenforceable due to Genentech's and/or COH's inequitable conduct before the PTO as set forth above.

161. MedImmune hereby seeks a declaratory judgment that the New Cabilly Patent is unenforceable.

*FOURTH CAUSE OF ACTION:*

*NON-INFRINGEMENT*

(Against Genentech and COH)

162. MedImmune incorporates the allegations of paragraphs 1 through 161 as if fully set forth herein.

163. An actual controversy has arisen and now exists between the parties concerning whether MedImmune's Synagis® product infringes any valid and enforceable claim of the New Cabilly Patent, but for the 1997 License Agreement.

164. MedImmune hereby seeks a declaratory judgment that, but for the 1997 License Agreement, its Synagis® product does not infringe any valid and enforceable claim of the New Cabilly Patent.

*FIFTH CAUSE OF ACTION:*

*SECTION 1 OF THE SHERMAN ACT*

(Against Genentech and Celltech)

165. MedImmune incorporates the allegations of paragraphs 1 through 164 as if fully set forth herein.

166. Genentech and Celltech conspired and reached the collusive Agreement that ultimately led to the improper issuance of the New Cabilly Patent.

167. Upon information and belief, the Agreement was entered into with the bad faith intent to harm competition.

168. The Agreement has a direct effect upon interstate trade or commerce.

169. Due to Genentech's and Celltech's anticompetitive behavior, MedImmune among others in the industry, has been harmed by either being blocked from the market altogether or by being required to make exorbitant payments for use of the

technology purportedly covered by the claims of the New Cabilly Patent.

170. The unlawful contract, combination, or conspiracy of Genentech and Celltech has no legitimate business objective and is a *per se* violation of Section 1 of the Sherman Act, 15 U.S.C. 1, *et seq.*

171. Upon information and belief, among other things, the Agreement is a market allocation agreement between horizontal competitors that is anticompetitive and illegal *per se* under Section 1 of the Sherman Act, 15 U.S.C. 1, *et seq.*

172. Alternatively, the unlawful contract, combination, or conspiracy of Genentech and Celltech unreasonably restrains competition in the relevant market and violates Section 1 of the Sherman Act under the Rule of Reason.

173. Genentech and Celltech are liable under Section 1 of the Sherman Act to MedImmune for damages in an amount to be proven at trial, including, without limitation, all payments made by MedImmune to Genentech on account of the New Cabilly Patent; which damages should be trebled under 15 U.S.C. § 15(a), plus interest, costs and expenses, including attorney fees.

*SIXTH CAUSE OF ACTION:*

*SECTION 2 OF THE SHERMAN ACT (CONSPIRACY TO MONOPOLIZE)*

(Against Genentech and Celltech)

174. MedImmune incorporates the allegations of paragraphs 1 through 173 as if fully set forth herein.

175. Genentech and Celltech conspired and reached the collusive Agreement that ultimately led to the improper issuance of the New Cabilly Patent.

176. Upon information and belief, the Agreement was entered into with the specific intent to grant a monopoly to Genentech that consists of the exclusive rights to what is asserted to be the fundamental technology embodied in the New Cabilly Patent.

177. The Agreement has a direct effect upon interstate trade or commerce.

178. Due to Genentech's and Celltech's anticompetitive behavior, MedImmune, among others in the industry, has been harmed by either being blocked from the market altogether or by being required to make exorbitant payments for use of the technology purportedly covered by the claims of the New Cabilly Patent.

179. The unlawful conspiracy of Genentech and Celltech violates Section 2 of the Sherman Act, 15 U.S.C. § 2, *et seq.*

180. Genentech and Celltech are liable under Section 2 of the Sherman Act to MedImmune for damages in an amount to be proven at trial, including, without limitation, all payments made by MedImmune to Genentech on account of the New Cabilly Patent; which damages should be trebled under 15 U.S.C. § 15(a), plus interest, costs and expenses, including attorney fees.

*SEVENTH CAUSE OF ACTION:*

*SECTION 2 OF THE SHERMAN ACT (MONOPOLIZATION BY GENENTECH)*

(Against Genentech)

181. MedImmune incorporates the allegations of paragraphs 1 through 180 as if fully set forth herein.

182. Upon information and belief, Genentech has monopoly power in the relevant market (as defined above).

183. Upon information and belief, Genentech willfully acquired and/or maintained its market dominance in the relevant market by anticompetitive means.

184. Genentech's willful acquisition and/or maintenance of its monopoly power by anticompetitive means has harmed MedImmune, among others in the industry, by either blocking them from the market altogether or requiring them to make exorbitant payments for use of the technology.

185. Genentech is liable under Section 2 of the Sherman Act to MedImmune for damages in an amount to be proven at trial, including, without limitation, all payments made to date by MedImmune to Genentech on account of the New Cabilly Patent; which damages should be trebled under 15 U.S.C. § 15(a), plus interest, costs and expenses, including attorney fees.

*EIGHTH CAUSE OF ACTION:*

*THE CARTWRIGHT ACT*
*(UNLAWFUL RESTRAINT OF TRADE)*

(Against Genentech and Celltech)

186. MedImmune incorporates the allegations of paragraphs 1 through 185 as if fully set forth herein.

187. Genentech and Celltech improperly conspired and reached the collusive Agreement that ultimately led to the improper issuance of the New Cabilly Patent.

188. Upon information and belief, the Agreement was entered into with the bad faith intent to harm competition.

189. The Agreement has a direct effect upon trade or commerce in California.

190. The collusive Agreement has no legitimate pro-competitive business objective and unreasonably harms competition.

191. Due to Genentech's and Celltech's anticompetitive behavior in violation of Section 16720 of the California Cartwright Act, MedImmune has been damaged by, for example, being required to make exorbitant payments for use of the New Cabilly Patent technology. Genentech and Celltech are liable to MedImmune for damages in an amount to be proven at trial; trebled under § 16750, plus interest, costs and expenses, including attorney fees.

*NINTH CAUSE OF ACTION:*

*THE CARTWRIGHT ACT*
*(CONSPIRACY TO MONOPOLIZE)*

(Against Genentech and Celltech)

192. MedImmune incorporates the allegations of paragraphs 1 through 191 as if fully set forth herein.

193. Genentech and Celltech conspired and reached the collusive Agreement that ultimately led to the improper issuance of the New Cabilly Patent.

194. Upon information and belief, the Agreement was entered into with the specific intent to grant a monopoly to Genentech that consists of the exclusive rights to what is asserted to be the fundamental technology embodied in the New Cabilly Patent.

195. The Agreement has a direct effect upon trade or commerce in California.

196. Due to Genentech's and Celltech's anticompetitive behavior, MedImmune, among others in the industry, has been harmed by either being blocked from the market altogether or by being required to make exorbitant payments for use of the technology purportedly covered by the claims of the New Cabilly Patent.

197. The unlawful conspiracy of Genentech and Celltech violates Sections 16720 *et seq.* of the California Cartwright Act.

198. Genentech and Celltech are liable under Section 16720 of the Cartwright Act to MedImmune for damages in an amount to be proven at trial, including, without limitation, all payments made to date by MedImmune to Genentech on account of the New Cabilly Patent; which damages should be trebled under § 16720, plus interest, costs and expenses, including attorney fees.

*TENTH CAUSE OF ACTION:*

*SECTION 17200 OF THE CALIFORNIA BUSINESS & PROFESSIONS CODE*

(Against Genentech and Celltech)

199. MedImmune incorporates the allegations of paragraphs 1 through 198 as if fully set forth herein.

200. Upon information and belief, Genentech and Celltech have colluded to obtain the issuance of the New Cabilly Patent, and have engaged in unfair, illegal or fraudulent business practices in violation of Section 17200 of the California Business & Professions Code. Due to the Defendants' unfair business practices, MedImmune has been required to make exorbitant payments for use of the New Cabilly Patent's technology.

201. Genentech and Celltech are liable to MedImmune for restitution of payments made to Genentech on account of the New Cabilly Patent, which payments are continuing, and Genentech should be enjoined from attempting to enforce the New Cabilly Patent and any of the terms of the collusive Agreement.

*PRAYER FOR RELIEF*

WHEREFORE, plaintiff MedImmune requests that judgment be entered in favor of MedImmune and against Defendants:

1. DECLARING that MedImmune has no obligation to pay royalties to Genentech under the License Agreements because the New Cabilly Patent is invalid and/or unenforceable and/or because MedImmune's sale of its Synagis® product does not infringe any valid claim of the New Cabilly Patent;

2. DECLARING that the New Cabilly Patent is invalid under 35 U.S.C. §§ 101, 102, 103, 112, *et seq.* and/or the judicially created doctrine of obviousness type double patenting;

3. DECLARING that MedImmune's sale of its Synagis® product does not infringe any valid and enforceable claim of the New Cabilly Patent;

4. DECLARING that the Agreement between Genentech and Celltech violates Section 1 of the Sherman Act;

5. DECLARING that the Agreement between Genentech and Celltech violates Section 2 of the Sherman Act;

6. DECLARING that the Agreement between Genentech and Celltech violates Section 17200 of the California Business & Professions Code;

7. DECLARING that the Agreement between Genentech and Celltech violates Section 16720 of the Cartwright Act;

8. ENJOINING Genentech and/or COH from enforcing the New Cabilly Patent;

9. AWARDING MedImmune actual and exemplary damages resulting from Genentech's and Celltech's anticompetitive use of the New Cabilly Patent, including, without limitation, treble damages under 15 U.S.C. § 15(a), Section

16750 of the California Cartwright Act, and such other exemplary damages as are available at law, including those available on account of Genentech's and Celltech's oppression, fraud, or malice; attorney fees; and costs; and

10. PROVIDING MedImmune such other and further relief as the Court may deem just and proper under the circumstances.

Dated: August 13, 2003

DEWEY BALLANTINE LLP

By: /s/ Jeffrey R. Witham
JEFFREY R. WITHAM
Attorneys for Plaintiff MEDIMMUNE, INC.

DEMAND FOR JURY TRIAL

Plaintiff MedImmune, Inc. hereby demands a jury trial as provided by Rule 38(a) of the Federal Rules of Civil Procedure.

DEWEY BALLANTINE LLP

By: /s/ Jeffrey R. Witham
JEFFREY R. WITHAM
Attorneys for Plaintiff MEDIMMUNE, INC.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

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CASE NO. CV03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff*,

v.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants*.

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# DEFENDANT GENENTECH, INC.'s ANSWER AND AFFIRMATIVE DEFENSES

## DEMAND FOR JURY TRIAL

Defendant Genentech, Inc. ("Genentech"), by its attorneys, hereby provides the following answer to the First Amended Complaint in this matter. Genentech notes that many of the allegations contained in the First Amended Complaint include false premises or assumptions and lack foundation. Thus, a denial of an allegation should be construed herein as a denial of the allegation itself, as well as any of its underlying and unsupported assumptions.

### *JURISDICTION AND VENUE*

1. Genentech admits that MedImmune, Inc. ("MedImmune") purports to seek declaratory relief pursuant to Fed. R. Civ. P. 57 and 28 U.S.C. §§ 2201 and 2202. Genentech admits that, based on the allegations, the Court has jurisdiction to hear this dispute, but denies that MedImmune is entitled to any relief or recovery whatsoever.

2. Genentech admits the allegation in paragraph 2.

*THE PARTIES*

3. Genentech admits that MedImmune, by and through its attorneys, purports to bring this action under antitrust, patent, and unfair competition laws against defendants Genentech, City of Hope ("COH"), and Celltech R&D Ltd. ("Celltech") (collectively, "Defendants") and that MedImmune purports to seek declaratory relief. Genentech denies that it engaged in any unlawful or improper conduct and denies that MedImmune is entitled to any relief or recovery whatsoever.

4. Genentech lacks sufficient information to answer the allegations in paragraph 4 and, on that basis, denies them.

5. Genentech admits that MedImmune sells a product under the name Synagis®. Genentech lacks sufficient information to answer the remaining allegations in paragraph 5 and, on that basis, denies them.

6. Genentech admits the allegations in paragraph 6.

7. Genentech admits on information and belief that COH is a California non-for-profit organization with its principal place of operation in Duarte, California. Genentech admits that COH is a co-assignee of the patent at issue in this case.

8. Genentech admits on information and belief that Celltech is a British company with its principal place of business in Slough, England. Genentech lacks sufficient information to answer the remaining allegations in paragraph 8 and, on that basis, denies them.

*SUMMARY OF THIS ACTION*

9. Genentech admits that MedImmune has purportedly filed this action to challenge an agreement between Genentech and Celltech and that MedImmune purports to seek declaratory relief. Genentech admits that it is a biotechnology company. Genentech admits that MedImmune purports to define "Agreement" in the manner alleged in paragraph 9 as

"an illegal and anticompetitive agreement." Genentech denies that it has entered into "an illegal and anticompetitive agreement" and denies that it engaged in any unlawful or improper conduct. Genentech further denies that MedImmune is entitled to the declaration it seeks or any other relief or recovery whatsoever. Genentech denies the remaining allegations in paragraph 9.

10. Genentech admits that it entered into certain agreements with Celltech to settle the case captioned *Genentech, Inc v. Celltech Therapeutics, Ltd.*, Case No. C-98-3926 MMC ("Civil Action") in the United States District Court for the Northern District of California, and to license certain rights to Celltech under U.S. Patent No. 6,331,415 B1 (the "'415 Patent"). Genentech further admits that the details of those agreements are confidential. Genentech denies the remaining allegations in paragraph 10.

11. Genentech admits that it was involved in a patent interference relating to U.S. Patent No. 4,816,397 (the "Boss Patent") and U.S. Patent Application No. 07/205,419 (the "'415 Patent Application"). Genentech admits that in the patent interference, it asserted that its assignors invented the same subject matter claimed by the Boss Patent before Celltech's assignors. Genentech admits that in the patent interference proceeding before the Patent and Trademark Office (Interference No. 102,572), the Board of Patent Appeals and Interferences ("PTO Board") ruled (incorrectly) in favor of Celltech regarding priority of invention. Genentech admits that it then filed the Civil Action pursuant to 35 U.S.C. § 146 to obtain judicial review of the PTO Board's ruling. Genentech admits that Judge Maxine M. Chesney denied two of Genentech's motions for summary adjudication in the Civil Action after concluding that there were triable issues of material fact. Genentech admits that, following Judge Chesney's suggestion that the parties resolve their dispute prior to trial, it entered into certain agreements with Celltech to settle

the Civil Action relating to the Boss Patent and the '415 Patent Application. Genentech denies the remaining allegations in paragraph 11.

12. Genentech admits that, prior to March 16, 2001, it entered into certain agreements with Celltech to settle legal proceedings relating to the Boss Patent and the '415 Patent Application, and asserts that these agreements speak for themselves. Genentech denies the remaining allegations in paragraph 12.

13. Genentech denies the allegations in paragraph 13 as they relate to it. Genentech lacks sufficient knowledge or information to admit or deny the allegations in paragraph 13 as they relate to Celltech and, on that basis, denies them.

14. Genentech denies the allegations in paragraph 14.

15. To the extent that this paragraph is deemed to relate to Celltech or other third parties, Genentech is without sufficient information to answer the allegations in paragraph 15 and, on that basis, denies them. To the extent that the paragraph relates to Genentech, Genentech denies the allegations in paragraph 15.

16. Genentech lacks sufficient information to answer the allegations in the first sentence in paragraph 16 and, on that basis, denies them. Genentech denies the allegations in the second sentence in paragraph 16.

17. Genentech admits that the term of the '415 Patent will expire in 2018. To the extent that this paragraph is deemed to relate to Celltech, Genentech is without sufficient information to answer the allegations in paragraph 17 and, on that basis, denies them. To the extent that the paragraph relates to Genentech, Genentech denies the allegations in paragraph 17.

18. Genentech admits that MedImmune has made payments to Genentech under a license agreement entered into between MedImmune and Genentech on or about June 5,

1997 ("1997 License Agreement"). Genentech admits that the 1997 License Agreement provided rights to various intellectual property, including the patent application that later matured into the '415 Patent. Genentech admits that Genentech and MedImmune entered into license agreements on or about February 7, 2003, that cover products that MedImmune has stated it is developing. Genentech denies the remaining allegations in paragraph 18.

19. Genentech admits that the First Amended Complaint purports to state claims under the cited statutes and legal theories. Genentech denies that it engaged in any unlawful or improper conduct and denies that MedImmune is entitled to any recovery whatsoever.

20. Genentech admits that the First Amended Complaint purports to seek declaratory relief. Genentech denies that it engaged in any unlawful or improper conduct denies that MedImmune is entitled to the declaration it seeks, or to any relief whatsoever.

21. Genentech admits that on April 8, 1983, a patent application listing Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel as inventors was filed in the United States Patent and Trademark Office. Genentech admits that application was given U.S. Patent Application Serial No. 06/483,457. Genentech admits that Messrs. Heynecker, Holmes, and Wetzel were affiliated with Genentech, and is informed and believes that Messrs. Cabilly and Riggs were affiliated with COH. Genentech further admits that Genentech and COH are co-assignees of both U.S. Patent No. 4,816,567 (the "'567 Patent") as well as the '415 Patent.

22. Genentech admits that the '567 Patent was issued on March 28, 1989, based on Patent Application Serial No. 06/483,457.

23. Genentech admits that on June 10, 1988, a continuation of U.S. Patent Application Serial No. 06/483,457 was filed, and that the continuation application was assigned US. Patent Application Serial No. 07/205,419.

24. Genentech admits that the PTO issued both the '567 Patent and U.S. Patent No. 4,816,397 on the same day, March 28, 1989.

25. Genentech admits that after the Boss Patent issued, Genentech amended U.S. Patent Application Serial No. 07/205,419 to copy claims from the Boss Patent to provoke an interference, based on the fact that Messrs. Cabilly, Heyneker, Holmes, Riggs, and Wetzel were the first inventors of the subject matter therein. Genentech admits that the PTO Board declared an interference between the Boss Patent and U.S. Patent Application Serial No. 07/205,419. Genentech denies the remaining allegations in paragraph 25.

26. Genentech admits that on February 28, 1991, the PTO Board declared Patent Interference No. 102,572 between certain claims of U.S. Patent Application Serial No. 07/205,419 and the claims of the Boss Patent. Genentech denies the remaining allegations in paragraph 26.

27. Genentech admits that the PTO Board declared Patent Interference No. 102,572 on February 28, 1991 and that the Board issued a final decision on August 13, 1998. Genentech admits that Genentech and Celltech made arguments to the Board regarding priority of invention. Genentech denies the remaining allegations in paragraph 27.

28. Genentech admits that on August 13, 1998, the PTO Board issued a final decision in Patent Interference No. 102,572 and refers to the decision for its terms. Genentech denies the remaining allegations in paragraph 28.

29. Genentech admits that on October 9, 1998, it commenced the Civil Action in order to obtain judicial review of the PTO Board's incorrect decision.

30. Genentech admits that the Civil Action was filed on October 9, 1998 and judgment was entered by the district court on March 16, 2001. Genentech admits that the Civil Action included depositions, document production, and expert disclosures.

31. Genentech admits that, during the course of the Civil Action, Dr. Cabilly located the draft patent application dated February 25, 1983. Genentech admits that Genentech made certain contentions regarding the draft patent application, including statements made in Genentech's summary adjudication papers filed in the Civil Action, and subject to any applicable protective order, refers to Genentech's motion papers for their content. Genentech denies the remaining allegations in paragraph 31.

32. Genentech admits that it moved for summary adjudication in the Civil Action and, subject to any applicable protective order, refers to Genentech's motion papers for their content. Genentech denies the remaining allegations in paragraph 32.

33. Genentech admits that Celltech opposed Genentech's motions for summary adjudication in the Civil Action, and, subject to any applicable protective order, refers to Celltech's motion papers for their content. Genentech denies the remaining allegations in paragraph 33.

34. Genentech admits that it filed reply briefs in support of its motions for summary adjudication, and, subject to any applicable protective order, refers to Genentech's reply briefs for their content. Genentech admits that Genentech filed a motion for summary adjudication that Celltech was not entitled to priority to the March 25, 1983 filing date of the British Boss patent application, and, subject to any applicable protective order, refers to Genentech's motion papers for their content. Genentech denies the remaining allegations in paragraph 34.

35. Genentech admits that it filed summary adjudication motions in the Civil Action, and that both it and Celltech filed papers in connection therewith, and, subject to any applicable protective order, refers to the motion papers for their content. Genentech denies the remaining allegations in paragraph 35.

36. Genentech admits that it entered into certain agreements with Celltech to settle the Civil Action after the district court denied Genentech's motions for summary adjudication on July 31, 2000. Genentech denies the remaining allegations in paragraph 36, and further denies that it engaged in any unlawful or improper conduct.

37. Genentech denies the allegations in paragraph 37, and further denies that it engaged in any unlawful or improper conduct.

38. To the extent that this paragraph is deemed to relate to Celltech, Genentech is without sufficient information to answer the allegations in paragraph 38 and, on that basis, denies them. To the extent that the paragraph relates to Genentech, Genentech denies the allegations in paragraph 38, and further denies that it engaged in any unlawful or improper conduct.

39. Genentech admits that in connection with their settlement agreement in the Civil Action, Genentech and Celltech submitted a proposed order to the District Court, and that the proposed order contained several proposed findings of fact and conclusions of law, including a proposed finding that "Genentech is entitled as a matter of law to priority over Celltech to invention described by the count." Genentech admits that Celltech opposed Genentech's motions for summary adjudication in the Civil Action, and, subject to any applicable protective order, refers to Celltech's motion papers for their content. Genentech denies the remaining allegations in paragraph 39.

40. Genentech denies the allegations in paragraph 40.

41. Genentech admits that Genentech and Celltech submitted a proposed order to the District Court and that the District Court signed an Order on March 16, 2001, and refers to the proposed order and Order for its content. Genentech denies the remaining allegations in paragraph 41, and further denies that it engaged in any unlawful or improper conduct.

42. Genentech admits that Genentech and Celltech submitted a proposed order to the District Court and that the District Court signed an Order on March 16, 2001, and refers to the proposed order and Order for its content.

43. Genentech admits that, following entry of the District Court's Judgment, the PTO Board issued a Final Order After District Court Judgment, and refers to the Final Order for its terms.

44. Genentech denies the allegations in paragraph 44, and further denies that it engaged in any unlawful or improper conduct.

45. Genentech admits that the PTO Board's Final Order After District Court Judgment contains a footnote which reads: "We will note that if a patent is issued to Cabilly, its term will begin to run now and the public has already been subject to patent rights of Boss since 1989, and that the interference has been pending since 1991." Genentech denies the remaining allegations in paragraph 45.

46. Genentech admits that the PTO Board issued a Final Order After District Court Judgment, and refers to the Final Order for its terms. Genentech denies the remaining allegations in paragraph 46.

47. Genentech admits that Celltech commenced a civil action captioned *Celltech R&D Ltd. v. Genentech, Inc.*, in the United States District Court for the Northern District of California pursuant to 35 U.S.C. § 146. To the extent that this paragraph is deemed to relate to Celltech, Genentech is

without sufficient information to answer the allegations in paragraph 47 and, on that basis, denies them. To the extent that the paragraph relates to Genentech, Genentech denies the remaining allegations in paragraph 47.

48. Genentech admits that the PTO Board ordered that the '415 Patent Application be forwarded to the patent examiner. Genentech denies the remaining allegations in paragraph 48.

49. Genentech denies the allegations in paragraph 49.

50. Genentech admits that after the PTO Board issued the Final Order After District Court Judgment, it ordered that the '415 Patent Application be forwarded to the patent examiner. Genentech denies the remaining allegations in paragraph 50.

51. Genentech denies the allegations in paragraph 51.

52. Genentech denies the allegations in paragraph 52.

53. Genentech admits that Celltech opposed Genentech's Motion for Summary Adjudication that Genentech Conceived of the Invention Described by the Count before March 25, 1983 in the Civil Action, and, subject to any applicable protective order, refers to Celltech's motion papers for their content. Genentech denies the remaining allegations in paragraph 53.

54. Genentech admits that Celltech opposed Genentech's Motion for Summary Adjudication that Genentech Conceived of the Invention Described by the Count before March 25, 1983 in the Civil Action, and, subject to any applicable protective order, refers to Celltech's motion papers for their content. Genentech denies the remaining allegations in paragraph 54.

55. Genentech admits that in the Civil Action it produced the Draft '415 Patent Application and, subject to any applicable protective order, refers to the Draft '415 Patent Application for its content. Genentech denies the remaining allegations of paragraph 55.

56. Genentech denies the allegations in paragraph 56.

57. Genentech admits that it filed a Motion for Summary Adjudication that Genentech Conceived of the Invention Described by the Count before March 25, 1983 in the Civil Action, and, subject to any applicable protective order, refers to Genentech's motion papers for their content. Genentech denies the remaining allegations in paragraph 57.

58. Genentech admits that it filed summary adjudication motions in the Civil Action and that Celltech opposed Genentech's motions for summary adjudication, and, subject to any applicable protective order, refers to Genentech's and Celltech's motion papers for their content. Genentech denies the remaining allegations in paragraph 58.

59. Genentech admits that it took a deposition of Dr. Weissman in the Civil Action and, subject to any applicable protective order, refers to the deposition transcript for its content. Genentech denies the remaining allegations in paragraph 59.

60. Genentech admits that it filed a Motion for Summary Adjudication that Celltech is Not Entitled to a Priority Date Based on its British Patent Application in the Civil Action, and, subject to any applicable protective order, refers to that motion for its content. Genentech denies the remaining allegations in paragraph 60.

61. Genentech admits that it filed a reply brief in support of its Motion for Summary Adjudication that Genentech Conceived of the Invention Described by the Count before March 25, 1983 and a Motion for Summary Adjudication that Celltech is Not Entitled to a Priority Date Based on its British Patent Application, and, subject to any applicable protective order, refers to those motion papers for their content. Genentech denies the remaining allegations in paragraph 61.

62. Genentech admits that it filed a Motion for Summary Adjudication that Genentech Conceived of the Invention Described by the Count before March 25, 1983 and a Motion for Summary Adjudication that Celltech is Not Entitled to a Priority Date Based on its British Patent Application, and, subject to any applicable protective order, refers to those motion papers for their content. Genentech denies the remaining allegations in paragraph 62.

63. Genentech admits that it filed a Motion for Summary Adjudication that Genentech Conceived of the Invention Described by the Count before March 25, 1983 and a Motion for Summary Adjudication that Celltech is Not Entitled to a Priority Date Based on its British Patent Application, and, subject to any applicable protective order, refers to those motion papers for their content. Genentech denies the remaining allegations in paragraph 63.

64. Genentech denies the allegations in paragraph 64, and further denies that it engaged in any unlawful or improper conduct.

65. Genentech denies the allegations in paragraph 65.

66. Genentech denies the allegations in paragraph 66, and further denies that it engaged in any unlawful or improper conduct.

67. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 67. Genentech denies that it engaged in any unlawful or improper conduct.

68. Genentech denies the allegations in paragraph 68, and further denies that it engaged in any unlawful or improper conduct.

69. Genentech denies the allegations in paragraph 69, and further denies that it engaged in any unlawful or improper conduct.

70. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 70.

71. Genentech admits that the District Court signed an Order on March 16, 2001, and refers to the Order for its content. Genentech further admits that, following entry of the District Court's Judgment, the PTO Board issued a Final Order After District Court Judgment, and refers to the Final Order for its terms. Genentech denies the remaining allegations in paragraph 71.

72. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of Paragraph 72.

73. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 73.

74. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 74.

75. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 75.

76. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 76.

77. Genentech denies the allegations in paragraph 77, and further denies that it engaged in any unlawful or improper conduct.

78. Genentech denies the allegations in paragraph 78, and further denies that it engaged in any unlawful or improper conduct.

79. Genentech denies the allegations in paragraph 79, and further denies that it engaged in any unlawful or improper conduct.

80. Genentech admits that it filed an Information Disclosure Statement ("IDS") dated September 18, 1991 with the PTO and refers to the IDS for its contents.

81. Genentech admits that it filed an IDS dated September 18, 1991 with the PTO, and refers to the IDS for its contents.

82. Genentech admits that it filed a paper in an April 19, 1994 Notice of Opposition proceeding (EP-B-0120694) before the European Patent Office, and, subject to any applicable protective order, refers to the paper for its contents. Genentech denies the remaining allegations in paragraph 82.

83. Genentech admits that it filed a paper in an April 19, 1994 Notice of Opposition proceeding (EP-B-0120694) before the European Patent Office, and, subject to any applicable protective order, refers to the paper for its contents. Genentech denies the remaining allegations in paragraph 83.

84. Genentech admits that it filed a paper in an April 19, 1994 Notice of Opposition proceeding (EP-B-0120694) before the European Patent Office, and, subject to any applicable protective order, refers to the paper for its contents. Genentech denies the remaining allegations in paragraph 84.

85. Genentech admits that it filed a paper in an April 19, 1994 Notice of Opposition proceeding (EP-B-0120694) before the European Patent Office, and, subject to any applicable protective order, refers to the paper for its contents.

Genentech further admits that it filed an IDS dated September 18, 1991 with the PTO, and refers to the IDS for its contents. Genentech denies the remaining allegations in paragraph 85.

86. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 86.

87. Genentech admits that the PTO Board issued a Final Order After District Court Judgment, and refers to the Final Order for its terms. Genentech admits that the PTO Board ordered that the '415 Patent Application be forwarded to the patent examiner. Genentech denies the remaining allegations in paragraph 87.

88. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 88.

89. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 89.

90. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 90.

91. Genentech denies the allegations in paragraph 91, and further denies that it engaged in any unlawful or improper conduct.

92. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 92.

93. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 93.

94. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 94.

95. Genentech denies the allegations in paragraph 95, and further denies that it engaged in any unlawful or improper conduct.

96. Genentech admits that it properly filed an IDS dated September 13, 2001, and refers to the IDS for its contents. Genentech denies the remaining allegations in paragraph 96, and further denies that it engaged in any unlawful or improper conduct.

97. Genentech admits that it filed an IDS dated September 13, 2001, and refers to the IDS for its contents. Genentech denies the remaining allegations in paragraph 97.

98. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 98.

99. Genentech denies the allegations in paragraph 99, and further denies that it engaged in any unlawful or improper conduct.

100. Genentech denies the allegations in paragraph 100, and further denies that it engaged in any unlawful or improper conduct.

101. Genentech denies the allegations in paragraph 101.

102. Genentech admits that it filed a complaint in the civil action captioned *Genentech, Inc. v. The Trustees of Columbia*

*University of the City of New York*, Case No. C 03-1603 VRW, in the United States District Court for the Northern District of California, and refers to the complaint for its contents. Genentech denies the remaining allegations in paragraph 102.

103. Genentech denies the allegations in paragraph 103.

104. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 104.

105. The prosecution history of the '415 Patent and documents therein speak for themselves. GNE denies that there was a failure to meet any obligations or duties that apply and further denies any other allegations of paragraph 105.

106. Genentech denies the allegations in paragraph 106, and further denies that it engaged in any unlawful or improper conduct.

107. Genentech admits that the '415 Patent issued on December 18, 2001. Genentech denies the remaining allegations in paragraph 107, and further denies that it engaged in any unlawful or improper conduct

108. Genentech admits the allegations in paragraph 108.

109. Genentech admits that the '415 Patent, in the abstract of the invention, contains the language: "processes for producing an immunoglobulin or an immunologically functional immunoglobulin fragment containing at least the variable domains of the immunoglobulin heavy and light chains. The processes can use on one or more vectors which produce both the heavy and light chains or fragments thereof in a single cell." Genentech further admits that one of its press releases states that the '415 Patent relates to "fundamental methods and compositions used to produce antibodies by recombinant

DNA technology," and that certain such antibody molecules can be used to provide beneficial treatment for certain illnesses.

110. To the extent that this paragraph is deemed to relate to Celltech, Genentech is without sufficient information to answer the allegations in paragraph 110 and, on that basis, denies them. To the extent that the paragraph relates to Genentech, Genentech denies the allegations in paragraph 110.

111. To the extent that this paragraph is deemed to relate to Celltech, Genentech is without sufficient information to answer the allegations in paragraph 111 and, on that basis, denies them. To the extent that the paragraph relates to Genentech, Genentech denies the allegations in paragraph 111.

112. Genentech admits that Genentech and Celltech properly filed their settlement agreement with the PTO under seal pursuant to applicable PTO rules and procedures. Genentech denies the remaining allegations in paragraph 112, and further denies that it engaged in any unlawful or improper conduct.

113. Genentech admits that, in a letter dated February 13, 2002, MedImmune requested a copy of Genentech and Celltech's agreement to settle the Civil Action. Genentech denies the remaining allegations in paragraph 113.

114. Genentech admits that, in a letter dated March 24, 2002, it responded to MedImmune's request for a copy of Genentech and Celltech's agreement to settle the Civil Action, and stated that: "The settlement agreement is a confidential document, and we cannot provide it to you." Genentech denies the remaining allegations in paragraph 114.

115. Genentech admits that, on May 8, 2002, MedImmune petitioned the PTO for access to the settlement agreement

between Celltech and Genentech in the Civil Action. Genentech admits that Genentech and Celltech opposed that petition. Genentech admits that the PTO denied MedImmune's petition. Genentech denies the remaining allegations in paragraph 115.

116. Genentech admits that various statements regarding the '415 Patent have been attributed to Genentech employees. Genentech further admits that the '415 Patent covers methods that come within its literal scope and are within the doctrine of equivalents as properly applied. Genentech denies the remaining allegations in paragraph 116.

117. Genentech admits that, in a letter dated January 7, 2002, Genentech confirmed to MedImmune its "expectation that MedImmune will pay royalties on sales of its Synagis antibody product pursuant to the license granted by Genentech under the recently issued U.S. Patent No. 6,331,415." Genentech denies any remaining allegations in paragraph 117.

118. Genentech admits that, in a letter dated February 13, 2002, MedImmune requested that Genentech advise it of Genentech's "basis for believing that MedImmune's product would infringe any valid claim of the '415 Patent such that royalties would be due." Genentech admits that, in that letter, MedImmune requested a copy of Genentech and Celltech's agreement to settle the Civil Action. Genentech denies the remaining allegations in paragraph 118.

119. Genentech admits that MedImmune "made the requested royalty payment" under the 1997 License Agreement and that, by letter dated March 8, 2002, MedImmune stated that "[s]uch payment, however, was made under protest and with reservation of all of our rights." Genentech admits that MedImmune continues to make royalty payments under the 1997 License Agreement on a quarterly basis. Genentech lacks sufficient information to answer the remaining allegations in paragraph 119 and, on that basis, denies them.

120. Genentech denies the allegations in paragraph 120.

121. Genentech admits that Celltech owned the Boss Patent. Genentech lacks sufficient information to answer the remaining allegations in paragraph 121 and, on that basis, denies them.

122. Genentech lacks sufficient information to answer the allegations in paragraph 122 and, on that basis, denies them.

123. To the extent that this paragraph is deemed to relate to Celltech, Genentech is without sufficient information to answer the allegations in paragraph 123 and, on that basis, denies them. To the extent that the paragraph relates to Genentech, Genentech admits that the '415 Patent will expire in 2018. Genentech denies the remaining allegations in paragraph 123.

124. To the extent that this paragraph is deemed to relate to Celltech, Genentech is without sufficient information to answer the allegations in paragraph 124 and, on that basis, denies them. To the extent that the paragraph relates to Genentech, Genentech admits that companies that wish to license the '415 Patent may do so and that, without a license, such companies are subject to U.S. Patent laws and thus not free to practice the claims of the '415 Patent as provided by those laws. Genentech denies the remaining allegations in paragraph 124.

125. To the extent that this paragraph is deemed to relate to Celltech, Genentech is without sufficient information to answer the allegations in paragraph 125 and, on that basis, denies them. Genentech admits that it entered into license agreements with MedImmune in 2003 under the '415 Patent to cover Vitaxin, Medi-507, and antibodies against Eph A2, IL-9, PC-Cell-Derived Growth Factor ("PCDGF"), Human Aspartyl (Asparaginyl) BetaHydroxylase ("HAAH"), and Human Metapneumovirus ("hMPV"). Genentech further admits that MedImmune has made payments to Genentech

under the 1997 License Agreement for certain sales of Synagis®. These payments were made, and the 2003 license agreements entered into, because MedImmune chose to practice one or more claims of the '415 Patent. Genentech denies the remaining allegations in paragraph 125.

126. Genentech does not understand this allegation and, on that basis, denies it.

127. Genentech is without sufficient information to form a belief as to the truth of the allegations in paragraph 127 and, on that basis, denies them.

128. Inasmuch as the allegations in paragraph 128 purport to state legal conclusions, no response thereto is required. To the extent a response is required, Genentech denies the allegations in paragraph 128.

129. Genentech denies the allegations in paragraph 129, and further denies that it engaged in any unlawful or improper conduct.

130. Genentech denies the allegations in paragraph 130, and further denies that it engaged in any unlawful or improper conduct.

*FIRST CAUSE OF ACTION*

*DECLARATORY JUDGMENT ON*

*CONTRACTUAL RIGHTS AND OBLIGATIONS*

(Against Genentech)

131. Genentech repeats and realleges its answers to paragraphs 1 through 130 above.

132. Inasmuch as the averments of paragraph 132 purport to state legal conclusions, no response thereto is required. Genentech denies that MedImmune is entitled to the relief it seeks, or to any relief, and further denies the remaining allegations in paragraph 132.

133. Genentech admits that MedImmune purports to seek declaratory relief, but denies that MedImmune is entitled to a declaratory judgment, or to any relief whatsoever.

*SECOND CAUSE OF ACTION*

*PATENT INVALIDITY*

(Against Genentech and COH)

134. Genentech repeats and realleges its answers to paragraphs 1 through 133 above.

135. Inasmuch as the averments of paragraph 135 purport to state legal conclusions, no response thereto is required. Genentech denies that MedImmune is entitled to the relief it seeks, or to any relief and further denies the remaining allegations in paragraph 135.

136. Genentech denies the allegations in paragraph 136.

137. Genentech denies the allegations in paragraph 137.

138. Genentech denies the allegations in paragraph 138.

139. Genentech admits that MedImmune purports to seek declaratory relief but denies that MedImmune is entitled to a declaratory judgment, or to any relief whatsoever.

*THIRD CAUSE OF ACTION*

*PATENT UNENFORCEABILITY*

(Against Genentech and COH)

140. Genentech repeats and realleges its answers to paragraphs 1 through 139 above.

141. Inasmuch as the averments of paragraph 141 purport to state legal conclusions, no response thereto is required. Genentech denies that MedImmune is entitled to the relief it seeks, or to any relief, and further denies the remaining allegations in paragraph 141.

142. Genentech denies the allegations in paragraph 142.

143. Genentech denies the allegations in paragraph 143, and further denies that it engaged in any unlawful or improper conduct.

144. Genentech denies the allegations in paragraph 144, and further denies that it engaged in any unlawful or improper conduct.

145. Genentech refers to and incorporates its answers to paragraphs 52-78. Genentech denies the remaining allegations in paragraph 145, and further denies that it engaged in any unlawful or improper conduct.

146. Genentech admits that it filed summary adjudication motions in the Civil Action and that Celltech opposed Genentech's motions for summary adjudication, and, subject to any applicable protective order, refers to Genentech's and Celltech's motion papers for their content. Genentech denies the remaining allegations in paragraph 146.

147. Genentech denies the allegations in paragraph 147.

148. Genentech refers to and incorporates its answers to paragraphs 52-78. Genentech denies the remaining allegations in paragraph 148.

149. Genentech refers to and incorporates its answers to paragraphs 79-91. Genentech denies the remaining allegations in paragraph 149.

150. Genentech refers to and incorporates its answers to paragraphs 79-91. Genentech denies the remaining allegations in paragraph 150, and further denies that it engaged in any unlawful or improper conduct.

151. Genentech refers to and incorporates its answers to paragraphs 92-99. Genentech denies the remaining allegations in paragraph 151, and further denies that it engaged in any unlawful or improper conduct.

152. Genentech refers to and incorporates its answers to paragraphs 92-99. Genentech denies the remaining allegations in paragraph 152, and further denies that it engaged in any unlawful or improper conduct.

153. Genentech refers to and incorporates its answers to paragraphs 100-106. Genentech denies the remaining allegations in paragraph 153, and further denies that it engaged in any unlawful or improper conduct.

154. Genentech refers to and incorporates its answers to paragraphs 100-106. Genentech denies the remaining allegations in paragraph 154, and further denies that it engaged in any unlawful or improper conduct.

155. Genentech denies the allegations in paragraph 155, and further denies that it engaged in any unlawful or improper conduct.

156. Genentech denies the allegations in paragraph 156, and further denies that it engaged in any unlawful or improper conduct.

157. Genentech denies the allegations in paragraph 157, and further denies that it engaged in any unlawful or improper conduct.

158. Genentech denies the allegations in paragraph 158, and further denies that it engaged in any unlawful or improper conduct.

159. Genentech denies the allegations in paragraph 159, and further denies that it engaged in any unlawful or improper conduct.

160. Genentech denies the allegations in paragraph 160.

161. Genentech admits that MedImmune purports to "seeks a declaratory judgment that the New Cabilly Patent is unenforceable," but denies that Genentech has committed any wrongful act or acts and denies that MedImmune is entitled to a declaratory judgment, or to any relief whatsoever.

*FOURTH CAUSE OF ACTION*

*NON-INFRINGEMENT*

(Against Genentech and COH)

162. Genentech repeats and realleges its answers to paragraphs 1 through 161 above.

163. Inasmuch as the averments of paragraph 163 purport to state legal conclusions, no response thereto is required. Genentech denies that MedImmune is entitled to the relief it seeks, or to any relief, and further denies the remaining allegations in paragraph 163.

164. Genentech admits that MedImmune purports to seek declaratory relief but denies that MedImmune is entitled to a declaratory judgment, or to any relief whatsoever.

*FIFTH CAUSE OF ACTION*

*SECTION 1 OF THE SHERMAN ACT*

(Against Genentech and Celltech)

165. Genentech repeats and realleges its answers to paragraphs 1 through 164 above.

166. Genentech denies the allegations in paragraph 166, and further denies that it engaged in any unlawful or improper conduct.

167. Genentech denies the allegations in paragraph 167, and further denies that it engaged in any unlawful or improper conduct.

168. Inasmuch as the averments of paragraph 168 purport to state legal conclusions, no response thereto is required. To the extent this paragraph avers facts, Genentech denies those averments.

169. Genentech denies the allegations in paragraph 169, and further denies that it engaged in any unlawful or improper conduct.

170. Genentech denies the allegations in paragraph 170, and further denies that it engaged in any unlawful or improper conduct.

171. Genentech denies the allegations in paragraph 171, and further denies that it engaged in any unlawful or improper conduct.

172. Genentech denies the allegations in paragraph 172, and further denies that it engaged in any unlawful or improper conduct.

173. Genentech denies the allegations of paragraph 173, and further denies that MedImmune is entitled to any relief or recovery whatsoever. Genentech notes that the Court has already dismissed, with prejudice, MedImmune's purported claim for unjust enrichment.

*SIXTH CAUSE OF ACTION*

*SECTION 2 OF THE SHERMAN ACT*

*(CONSPIRACY TO MONOPOLIZE)*

(Against Genentech and Celltech)

174. Genentech repeats and realleges its answers to paragraphs 1 through 173 above.

175. Genentech denies the allegations in paragraph 175, and further denies that it engaged in any unlawful or improper conduct.

176. Genentech denies the allegations in paragraph 176, and further denies that it engaged in any unlawful or improper conduct.

177. Inasmuch as the averments of paragraph 177 purport to state legal conclusions, no response thereto is required. To the extent this paragraph avers facts, Genentech denies those averments.

178. Genentech denies the allegations in paragraph 178.

179. Genentech denies the allegations in paragraph 179, and further denies that it engaged in any unlawful or improper conduct.

180. Genentech denies the allegations in paragraph 180, and further denies that MedImmune is entitled to any recovery or relief whatsoever. Genentech notes that the Court has already dismissed, with prejudice, MedImmune's purported claim for unjust enrichment

*SEVENTH CAUSE OF ACTION*

*SECTION 2 OF THE SHERMAN ACT*

*(MONOPOLIZATION BY GENENTECH)*

(Against Genentech)

181. Genentech repeats and realleges its answers to paragraphs 1 through 180 above.

182. Genentech denies the allegations in paragraph 182.

183. Genentech denies the allegations in paragraph 183, and further denies that it engaged in any unlawful or improper conduct.

184. Genentech denies the allegations in paragraph 184, and further denies that it engaged in any unlawful or improper conduct.

185. Genentech denies the allegations in paragraph 185, and further denies that MedImmune is entitled to any recovery or relief whatsoever. Genentech notes that the Court has already dismissed, with prejudice, MedImmune's purported claim for unjust enrichment.

*EIGHTH CAUSE OF ACTION*

*TEE CARTWRIGHT ACT*

*(UNLAWFUL RESTRAINT OF TRADE)*

(Against Genentech and Celltech)

186. Genentech repeats and realleges its answers to paragraphs 1 through 185 above.

187. Genentech denies the allegations in paragraph 187, and further denies that it engaged in any unlawful or improper conduct.

188. Genentech denies the allegations in paragraph 188, and further denies that it engaged in any unlawful or improper conduct.

189. Inasmuch as the averments of paragraph 189 purport to state legal conclusions, no response thereto is required. To the extent this paragraph avers facts, Genentech denies those averments.

190. Genentech denies the allegations in paragraph 190.

191. Genentech denies the allegations in paragraph 191, and further denies that MedImmune is entitled to any recovery or relief whatsoever. Genentech notes that the Court has already dismissed, with prejudice, MedImmune's purported claim for unjust enrichment

*NINTH CAUSE OF ACTION*

*THE CARTWRIGHT ACT*

*(CONSPIRACY TO MONOPOLIZE)*

(Against Genentech and Celltech)

192. Genentech repeats and realleges its answers to paragraphs 1 through 191 above.

193. Genentech denies the allegations in paragraph 193, and further denies that it engaged in any unlawful or improper conduct.

194. Genentech denies the allegations in paragraph 194, and further denies that it engaged in any unlawful or improper conduct.

195. Inasmuch as the averments of paragraph 195 purport to state legal conclusions, no response thereto is required. To the extent this paragraph avers facts, Genentech denies those averments.

196. Genentech denies the allegations in paragraph 196, and further denies that it engaged in any unlawful or improper conduct.

197. Genentech denies the allegations in paragraph 197, and further denies that it engaged in any unlawful or improper conduct.

198. Genentech denies the allegations in paragraph 198, and further denies that MedImmune is entitled to any recovery or relief whatsoever. Genentech notes that the Court has already dismissed, with prejudice, MedImmune's purported claim for unjust enrichment.

*TENTH CAUSE OF ACTION*

*SECTION 17200 OF*

*THE CALIFORNIA BUSINESS AND PROFESSIONS CODE*

(Against Genentech and Celltech)

199. Genentech repeats and realleges its answers to paragraphs 1 through 198 above.

200. Genentech denies the allegations in paragraph 200, and further denies that it engaged in any unlawful or improper conduct.

201. Genentech denies the allegations in paragraph 201, and further denies that MedImmune is entitled to any recovery or relief whatsoever. Genentech notes that the Court has already dismissed, with prejudice, MedImmune's purported claim for unjust enrichment.

WHEREFORE, defendant Genentech denies that plaintiff is entitled to any relief whatsoever and respectfully requests judgment dismissing the complaint with prejudice and with costs and attorneys' fees, as may be allowed by law, and such further relief as the Court deems appropriate.

Defendant Genentech denies each and every allegation of the complaint not specifically herein admitted.

*AFFIRMATIVE DEFENSES*

Genentech states the following affirmative defenses without assuming the burden of proof on such defenses that would otherwise rest on plaintiff.

*First Affirmative Defense*

The First Amended Complaint, and each claim for relief, fails to state a claim upon which relief may be granted.

*Second Affirmative Defense*

Plaintiff failed to mitigate any damages purportedly suffered as a result of the conduct alleged in the complaint.

*Third Affirmative Defense*

Plaintiff's claims are barred, in whole or in part because any conduct engaged in by Genentech has been reasonable and based on independent, legitimate business and economic justifications, without any purpose or intent to injure competition.

*Fourth Affirmative Defense*

Plaintiff's claims are barred, in whole or in part, by the competition privilege.

*Fifth Affirmative Defense*

Each of the claims in the complaint, in whole or in part, is barred by the doctrines of waiver, laches, and estoppel.

*Sixth Affirmative Defense*

Each of the claims in the complaint, in whole or in part, is barred by the doctrine of unclean hands.

*Seventh Affirmative Defense*

Plaintiff's claims are barred to the extent that Plaintiff's purported injuries and damages were not proximately caused by acts or omissions of Genentech. There is no causal relationship between the losses alleged, if any, and any alleged wrongful acts or omissions by Genentech.

*Eighth Affirmative Defense*

Plaintiff's claims are barred, in whole or in part, by the applicable statutes of limitation.

*Ninth Affirmative Defense*

Any injury suffered by the plaintiff is not an injury which the antitrust laws are designed to prevent, or which flows from anything which would make Genentech's alleged conduct unlawful under the patent or antitrust laws.

*Tenth Affirmative Defense*

Plaintiff has waived each of the claims alleged in the complaint, in whole or in part.

*Eleventh Affirmative Defense*

Some or all of Genentech's conduct challenged by plaintiff is protected conduct under the *Noerr-Pennington* Doctrine, the First Amendment, and/or other related doctrines.

*Twelfth Affirmative Defense*

Plaintiff's claims are barred to the extent that plaintiff's claimed injuries and damages were not proximately caused by any acts or omissions of Genentech.

*Thirteenth Affirmative Defense*

Plaintiff has an adequate remedy at law and no basis exists for the grant of equitable relief.

*Fourteenth Affirmative Defense*

The Second, Third, and Fourth causes of action are barred by the U.S. patent laws.

*Fifteenth Affirmative Defense*

Plaintiff lacks standing to bring the causes of action asserted in the First Amended Complaint.

*Sixteenth Affirmative Defense*

Genentech hereby adopts and incorporates by this reference any and all other affirmative defenses asserted or to be asserted by any other defendant in this proceeding to the extent that defendants may share in such affirmative defenses.

*Seventeenth Affirmative Defense*

Genentech has not knowingly and intentionally waived any applicable affirmative defense and reserves the right to raise additional affirmative defenses as they become known to it through discovery in this matter. Genentech further reserves the right to amend its answer and/or affirmative defenses accordingly and/or to delete affirmative defenses that it determines are not applicable during the course of subsequent discovery.

*PRAYER FOR RELIEF*

WHEREFORE Genentech requests relief as follows:

1. That MedImmune's claims be dismissed with prejudice;

2. That MedImmune take nothing by reason of its First Amended Complaint;

3. That MedImmune's request for injunctive relief be denied;

4. For the cost of this suit, including reasonable attorney's fees and interest; and

5. For such other and further relief as the Court may deem proper.

Dated: September 2, 2003 Respectfully submitted,

LATHAM & WATKINS LLP
Daniel M. Wall
Mark A. Flagel
Dean G. Dunlavey
James K. Lynch

By: /s/ Mark A. Flagel
Mark A. Flagel
Genentech, Inc.

DEMAND FOR JURY TRIAL

Genentech hereby demands a trial by jury for all issues so triable in this action.

Dated: September 2, 2003 Respectfully submitted,

LATHAM & WATKINS LLP
Daniel M. Wall
Mark A. Flagel
Dean G. Dunlavey
James K. Lynch

By: /s/ Mark A. Flagel
MARK A. FLAGEL
Attorneys for Defendant
Genentech, Inc.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

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Case No. CV-03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

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# DEFENDANT CITY OF HOPE NATIONAL MEDICAL CENTER'S ANSWER

## DEMAND FOR JURY TRIAL

Defendant City of Hope, by counsel, hereby answers the First Amended Complaint filed by Plaintiff MedImmune, Inc. ("MedImmune"), and states as follows. The numbered paragraphs herein correspond to the numbered paragraphs of the First Amended Complaint.

1. City of Hope admits that the First Amended Complaint purports to state a claim for declaratory relief pursuant to Fed. R. Civ. P. 57 and 28 U.S.C. §§ 2201 and 2202. City of Hope admits that it is organized under the laws of the state of California and that its principal place of operation is in California. City of Hope further admits that Genentech, Inc. has its principal place of business in California and that Celltech filed a complaint in the United States District Court for the Northern District of California captioned *Celltech R&D Ltd. v. Genentech, Inc.*, Civ. Act. 01-3560 JCS. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 1 of the First Amended Complaint, and therefore denies them.

except that inasmuch as the allegations of jurisdiction purport to state legal conclusions, no response thereto is required.

2. Because the allegation of venue in paragraph 2 of the First Amended Complaint purports to state legal conclusions, no response thereto is required.

3. City of Hope admits that the First Amended Complaint purports to state claims under the legal theories cited in paragraph 3, but denies that MedImmune is entitled to any relief under those theories. City of Hope denies the other allegations of paragraph 3 of the First Amended Complaint.

4. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 4 of the First Amended Complaint, and therefore denies them.

5. City of Hope admits that MedImmune sells a product under the name Synagis. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 5 of the First Amended Complaint, and therefore denies them.

6. City of Hope admits the allegations of paragraph 6 of the First Amended Complaint.

7. City of Hope admits the allegations of paragraph 7 of the First Amended Complaint.

8. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 8 of the First Amended Complaint, and therefore denies them.

9. City of Hope admits that the First Amended Complaint includes a claim for declaratory relief, but denies that MedImmune is entitled to any such relief. City of Hope denies the other allegations of paragraph 9 of the First Amended Complaint.

10. City of Hope admits that Celltech and Genentech altered into an agreement or agreements (collectively, the "Agreement"). City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 10 of the First Amended Complaint, and therefore denies them.

11. City of Hope admits that Celltech and Genentech entered into the Agreement and the terms of that Agreement will speak for itself. City of Hope further admits that Celltech and Genentech were involved in an interference in the PTO that was resolved in favor Celltech. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 11 of the First Amended Complaint, and therefore denies them.

12. City of Hope admits that Celltech and Genentech entered into the Agreement prior to March 16, 2001. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 12 of the First Amended Complaint, and therefore denies them.

13. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 13 of the First Amended Complaint, and therefore denies them.

14. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 14 of the First Amended Complaint, and therefore denies them.

15. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 15 of the First Amended Complaint, and therefore denies them.

16. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 16 of the First Amended Complaint, and therefore denies them.

17. City of Hope admits that the U.S. Patent No. 6,331,415 BI (the "New Cabilly Patent") will expire in 2018. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 17 of the First Amended Complaint, and therefore denies them.

18. City of Hope admits that MedImmune makes payments to Genentech under a 1997 License Agreement, and that the 1997 License Agreement will speak for itself. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 18 of the First Amended Complaint, and therefore denies them.

19. City of Hope admits that the First Amended Complaint purports to state claims under the cited statutes and legal theories, but denies that MedImmune is entitled to any such relief. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 19 of the First Amended Complaint, and therefore denies them.

20. City of Hope admits that the First Amended Complaint seeks declaratory relief but denies that MedImmune is entitled to any such relief. City of Hope denies the remaining allegations of paragraph 20.

21. City of Hope admits the allegations of paragraph 21 of the First Amended Complaint.

22. City of Hope admits that the '567 patent was issued on March 28, 1989, based on Patent Application Serial No. 06/483,457.

23. City of Hope admits that a continuation of U.S. Patent Application Serial No. 06/483,457 was filed on June 10, 1988, and that it was assigned U.S. Patent Application Serial No. 07/205,419.

24. City of Hope admits the allegation of paragraph 24 of the First Amended Complaint.

25. City of Hope admits that the PTO Board of Patent Interferences and Appeals (the "PTO Board") initiated an interference proceeding to determine priority of invention between U.S. Patent Application No. 07/205,419 (the "New Cabilly Application") and U.S. Patent No. 4,816,397 (the "Boss Patent"). City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 25 of the First Amended Complaint, and therefore denies them.

26. City of Hope admits that on February 28, 1991, the PTO Board declared Patent Interference No. 102,572 between certain claims of the New Cabilly Application and the Boss Patent. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 26 of the First Amended Complaint, and therefore denies them.

27. City of Hope admits that Patent Interference No. 102,572 was declared on February 28, 1991, that the final decision of the PTO Board was issued on August 13, 1998 and that Genentech and Celltech made arguments to the PTO Board about priority. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 27 of the First Amended Complaint, and therefore denies them.

28. City of Hope admits that the PTO Board issued a final decision on August 13, 1998 and that final decision speaks for itself. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations

of paragraph 28 of the First Amended Complaint, and therefore denies them.

29. City of Hope admits that, on October 9, 1998, Genentech initiated a civil action under 35 U.S.C. § 146 entitled *Genentech, Inc. v. Celltech R&D Ltd.*, Case No. C98-3926 MMC (the "Civil Action"), in the United States District Court for the Northern District of California. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 29 of the First Amended Complaint, and therefore denies them.

30. City of Hope admits that the Civil Action was filed on October 9, 1998 and judgment was entered by the district court on March 16, 2001. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 30 of the First Amended Complaint, and therefore denies them.

31. City of Hope admits that Schmuel Cabilly had in his possession a draft patent application (the "Draft Cabilly Application") dated February 25, 1983, that Genentech asserted contentions about the Draft Cabilly Application including in its summary adjudication motion, and that Genentech's statements speak for themselves. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 31 of the First Amended Complaint, and therefore denies then.

32. City of Hope admits the Genentech moved for summary adjudication in the Civil Action and that Genentech's motion papers speak for themselves. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 32 of the First Amended Complaint, and therefore denies them.

33. City of Hope admits that Celltech opposed Genentech's motion for summary judgment in the Civil Action and that Celltech's opposition papers speak for themselves. City

of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 33 of the First Amended Complaint, and therefore denies them.

34. City of Hope admits that Genentech filed a reply brief in support of its motion for summary judgment and that Genentech's reply brief speaks for itself. City of Hope further admits that Genentech moved for summary adjudication that Celltech was not entitled to the March 25, 1983 priority date and that Genentech's motion papers speak for themselves. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 34 of the First Amended Complaint, and therefore denies them.

35. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 35 of the First Amended Complaint, and therefore denies them. Insofar as the allegations of paragraph 35 purport to state legal conclusions, no response thereto is required.

36. City of Hope admits that Genentech and Celltech entered into the Agreement. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 36 of the First Amended Complaint, and therefore denies them. Insofar as the allegations of paragraph 35 purport to state legal conclusions, no response thereto is required.

37. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 37 of the First Amended Complaint, and therefore denies them. Insofar as the allegations of paragraph 37 purport to state legal conclusions, no response thereto is required.

38. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 38 of the First Amended Complaint, and therefore denies them. Insofar as the allegations of paragraph 38 purport to state legal conclusions, no response thereto is required.

39. City of Hope admits that Genentech and Celltech submitted a proposed order to the District Court, and that proposed order speaks for itself. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 39 of the First Amended Complaint, and therefore denies them.

40. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 40 of the First Amended Complaint, and therefore denies them. Insofar as the allegations of paragraph 40 purport to state legal conclusions, no response thereto is required.

41. City of Hope admits that the District Court issued an order on March 16, 2001 and that the order and Genentech's and Celltech's proposed order speak for themselves. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 41 of the First Amended Complaint, and therefore denies them.

42. City of Hope admits that there is an order dated March 16, 2001 and that order speaks for itself. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 42 of the First Amended Complaint, and therefore denies them.

43. City of Hope admits that, following entry of the District Court's judgment, the PTO Board issued a Final Order After District Court Judgment, and that PTO Board order speaks for itself. City of Hope lacks sufficient knowledge to

form a belief or understanding as to the truth of the other allegations of paragraph 43 of the First Amended Complaint, and therefore denies them.

44. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 44 of the First Amended Complaint, and therefore denies them.

45. City of Hope admits that the PTO Board issued a Final Order After District Court Judgment and that the PTO Board order speaks for itself. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 45 of the First Amended Complaint, and therefore denies them.

46. City of Hope admits that the PTO Board issued a Final Order After District Court Judgment and that the PTO Board order speaks for itself. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 46 of the First Amended Complaint, and therefore denies them.

47. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 47 of the First Amended Complaint, and therefore denies them.

48. City of Hope admits that the PTO Board referred the New Cabilly Application to a patent examiner to continue prosecution. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 48 of the First Amended Complaint, and therefore denies them.

49. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 49 of the First Amended Complaint, and therefore denies them.

50. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 50 of the First Amended Complaint, and therefore denies them.

51. City of Hope denies the allegations of paragraph 51 of the First Amended Complaint

52. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 52 of the First Amended Complaint, and therefore denies them.

53. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 53 of the First Amended Complaint, and therefore denies them.

54. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 54 of the First Amended Complaint, and therefore denies them.

55. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 54 of the First Amended Complaint, and therefore denies them.

56. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 56 of the First Amended Complaint, and therefore denies them.

57. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 57 of the First Amended Complaint, and therefore denies them.

58. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 58 of the First Amended Complaint, and therefore denies them.

59. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 59 of the First Amended Complaint, and therefore denies them.

60. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 60 of the First Amended Complaint, and therefore denies them.

61. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 61 of the First Amended Complaint, and therefore denies them.

62. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope denies that the Draft Cabilly Application was not enabling. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 62 of the First Amended Complaint, and therefore denies them.

63. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope denies that the Cabilly Patent is not entitled to priority of invention. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 63 of the First Amended Complaint, and therefore denies than.

64. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope denies that Draft Cabilly Application was not enabling. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 64 of the First Amended Complaint, and therefore denies them.

65. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a

response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 65 of the First Amended Complaint, and therefore denies them.

66. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 66 of the First Amended Complaint, and therefore denies them.

67. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope denies that there were defects in the enablement of the invention. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 67 of the First Amended Complaint, and therefore denies them.

68. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 68 of the First Amended Complaint, and therefore denies them.

69. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 69 of the First Amended Complaint, and therefore denies them.

70. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 70 of the First Amended Complaint, and therefore denies them.

71. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 71 of the First Amended Complaint, and therefore denies them.

72. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 72 of the First Amended Complaint, and therefore denies them.

73. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 73 of the First Amended Complaint, and therefore denies them.

74. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 74 of the First Amended Complaint, and therefore denies them.

75. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 75 of the First Amended Complaint, and therefore denies them.

76. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 76 of the First Amended Complaint, and therefore denies them.

77. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 77 of the First Amended Complaint, and therefore denies them.

78. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 78 of the First Amended Complaint, and therefore denies them.

79. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 79 of the First Amended Complaint, and therefore denies them.

80. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope admits that Genentech filed an Information Disclosure Statement ("IDS") dated September 18, 1991 and that the IDS speaks for itself. City of Hope lacks sufficient knowledge as to the truth of the other allegations of paragraph 78 of the First Amended Complaint, and therefore denies than.

81. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 81 of the First Amended Complaint, and therefore denies them.

82. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 82 of the First Amended Complaint, and therefore denies them.

83. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 83 of the First Amended Complaint, and therefore denies them.

84. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a

belief or understanding as to the truth of the allegations of paragraph 84 of the First Amended Complaint, and therefore denies them.

85. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 85 of the First Amended Complaint, and therefore denies them.

86. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 86 of the First Amended Complaint, and therefore denies them.

87. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 87 of the First Amended Complaint, and therefore denies them.

88. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 88 of the First Amended Complaint, and therefore denies them.

89. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a

response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 89 of the First Amended Complaint, and therefore denies them.

90. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 90 of the First Amended Complaint, and therefore denies them.

91. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 91 of the First Amended Complaint, and therefore denies them.

92. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 92 of the First Amended Complaint, and therefore denies them.

93. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 93 of the First Amended Complaint, and therefore denies them.

94. These allegations do not relate to City of Hope and contain legal conclusions and therefore require no response.

To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 94 of the First Amended Complaint, and therefore denies them.

95. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 95 of the First Amended Complaint, and therefore denies them.

96. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope denies the allegations of paragraph 96 of the First Amended Complaint.

97. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 97 of the First Amended Complaint, and therefore denies them.

98. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 98 of the First Amended Complaint, and therefore denies them.

99. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a

response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 99 of the First Amended Complaint, and therefore denies them.

100. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 100 of the First Amended Complaint, and therefore denies them.

101. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 101 of the First Amended Complaint, and therefore denies them.

102. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 102 of the First Amended Complaint, and therefore denies them.

103. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the troth of the allegations of paragraph 103 of the First Amended Complaint, and therefore denies them.

104. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is

deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 104 of the First Amended Complaint, and therefore denies them.

105. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 105 of the First Amended Complaint, and therefore denies them.

106. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 106 of the First Amended Complaint, and therefore denies them.

107. City of Hope admits that the New Cabilly Patent issued on December 18, 2001. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 107 of the First Amended Complaint, and therefore denies them.

108. City of Hope admits that the New Cabilly Patent issued, and that it speaks for itself.

109. City of Hope admits that the New Cabilly Patent issued, and that it speaks for itself. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 109 of the First Amended Complaint, and therefore denies them.

110. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is

deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 110 of the First Amended Complaint, and therefore denies them.

111. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 111 of the First Amended Complaint, and therefore denies them.

112. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 112 of the First Amended Complaint, and therefore denies them, except that insofar as the allegations of paragraph 112 purport to state legal conclusions, no response thereto is required.

113. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 113 of the First Amended Complaint, and therefore denies them.

114. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 114 of the First Amended Complaint, and therefore denies them.

115. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 115 of the First Amended Complaint, and therefore denies them.

116. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 116 of the First Amended Complaint, and therefore denies them.

117. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 117 of the First Amended Complaint, and therefore denies them.

118. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 118 of the First Amended Complaint, and therefore denies them.

119. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope admits that MedImmune makes royalty payments to Genentech. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of

the other allegations of paragraph 119 of the First Amended Complaint, and therefore denies them.

120. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 120 of the First Amended Complaint, and therefore denies them.

121. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 121 of the First Amended Complaint, and therefore denies them.

122. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 122 of the First Amended Complaint, and therefore denies them.

123. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 123 of the First Amended Complaint, and therefore denies them.

124. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope admits that Genentech has the right to

issue licenses under the New Cabilly Patent that may result in royalty payments. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the other allegations of paragraph 124 of the First Amended Complaint, and therefore denies them.

125. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 125 of the First Amended Complaint, and therefore denies them.

126. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 126 of the First Amended Complaint, and therefore denies them.

127. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 127 of the First Amended Complaint, and therefore denies them.

128. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 128 of the First Amended Complaint, and therefore denies them.

129. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 129 of the First Amended Complaint, and therefore denies them. Insofar as the allegations of paragraph 129 purport to state legal conclusions, no response thereto is required.

130. These allegations do not relate to City of Hope and therefore require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 130 of the First Amended Complaint, and therefore denies them, except that insofar as the allegations of paragraph 130 purport to state legal conclusions, no response thereto is required.

*FIRST CAUSE OF ACTION:*

*DECLARATORY JUDGMENT ON CONTRACTUAL RIGHTS AND OBLIGATIONS*

(Against Genentech)

131. In response to the allegations of paragraph 131 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-130 as if fully set forth herein.

132. Inasmuch as the allegations of paragraph 132 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 132 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

133. Inasmuch as the allegations of paragraph 133 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 133 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

*SECOND CAUSE OF ACTION:*

*PATENT INVALIDITY*

(Against Genentech and City of Hope)

134. In response to the allegations of paragraph 134 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-133 as if fully set forth herein.

135. City of Hope denies the allegations of paragraph 135.

136. City of Hope denies the allegations of paragraph 136.

137. City of Hope denies the allegations of paragraph 137.

138. City of Hope denies the allegations of paragraph 138.

139. City of Hope admits that MedImmune seeks declaratory judgment, but denies that MedImmune is entitled to such relief.

*THIRD CAUSE OF ACTION:*

*PATENT UNENFORCEABILITY*

(Against Genentech and City of Hope)

140. In response to the allegations of paragraph 140 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-139 as if fully set forth herein.

141. City of Hope denies the allegations of paragraph 141 of the First Amended Complaint.

142. City of Hope denies the allegations of paragraph 142 of the First Amended Complaint.

143. City of Hope denies the allegation of paragraph 143 of the First Amended Complaint.

144. City of Hope denies the allegation of paragraph 144 of the First Amended Complaint.

145. City of Hope incorporates its answers to paragraphs 52 through 78. City of Hope denies the other allegation of paragraph 145 of the First Amended Complaint.

146. To the extent these allegations do not relate to City of Hope, they require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope denies that the Draft Cabilly Application lacked enabling disclosure of the claimed invention. City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth the other allegations of paragraph 146 of the First Amended Complaint, and therefore denies them.

147. City of Hope denies the allegations of paragraph 147 of the First Amended Complaint.

148. City of Hope denies the allegations of paragraph 148 of the First Amended Complaint.

149. City of Hope incorporates its answers to paragraphs 79 through 91. City of Hope denies the other allegations of paragraph 149 of the First Amended Complaint.

150. City of Hope incorporates its answers to paragraphs 79 through 91. City of Hope denies the other allegations of paragraph 150 of the First Amended Complaint.

151. City of Hope incorporates its answers to paragraphs 92 through 99. City of Hope denies the other allegations of Paragraph 151 of the First Amended Complaint.

152. City of Hope incorporates its answers to paragraphs 92 through 99. City of Hope denies the other allegations of paragraph 152 of the First Amended Complaint.

153. City of Hope incorporates its answers to paragraphs 100 through 106. City of Hope denies the other allegations of paragraph 153 of the First Amended Complaint.

154. City of Hope incorporates its answers to paragraphs 100 through 106. City of Hope denies the other allegations of paragraph 154 of the First Amended Complaint.

155. City of Hope denies the allegation of paragraph 155 of the First Amended Complaint.

156. To the extent these allegations do not relate to City of Hope, they require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 156 of the First Amended Complaint, and therefore denies them.

157. To the extent these allegations do not relate to City of Hope, they require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 157 of the First Amended Complaint, and therefore denies them.

158. To the extent these allegations do not relate to City of Hope, they require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require a response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 158 of the First Amended Complaint, and therefore denies them.

159. To the extent these allegations do not relate to City of Hope, they require no response. To the extent this paragraph is deemed to relate to City of Hope or otherwise to require response, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations of paragraph 159 of the First Amended Complaint, and therefore denies them.

160. City of Hope denies the allegations of paragraph 160 of the First Amended Complaint.

161. City of Hope admits that MedImmune seeks declaratory judgment, but denies that MedImmune is entitled to such relief.

*FOURTH CAUSE OF ACTION:*

*NON-INFRINGEMENT*

(Against Genentech and City of Hope)

162. In response to the allegations of paragraph 162 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-161 as if fully set forth herein.

163. City of Hops denies the allegations of paragraph 163 of the First Amended Complaint.

164. City of Hope admits that MedImmune seeks declaratory judgment, but denies that MedImmune is entitled to such relief.

*FIFTH CAUSE OF ACTION:*

*SECTION 1 OF THE SHERMAN ACT*

(Against Genentech and Celltech)

165. In response to the allegations of paragraph 165 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-164 as if fully set forth herein.

166. Inasmuch as the allegations of paragraph 166 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 166 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

167. Inasmuch is the allegations of paragraph 167 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 167 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

168. Inasmuch as the allegations of paragraph 168 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 168 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

169. Inasmuch as the allegations of paragraph 169 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 169 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

170. Inasmuch as the allegations of paragraph 170 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 170 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

171. Inasmuch as the allegations of paragraph 171 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 171 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

172. Inasmuch the allegations of paragraph 172 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 172 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

173. Inasmuch as the allegations of paragraph 173 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 173 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

*SIXTH CAUSE OF ACTION:*

*SECTION 2 OF THE SHERMAN ACT*
*CONSPIRACY TO MONOPOLY*

(Against Genentech and Celltech)

174. In response to the allegations of paragraph 174 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-173 as if fully set forth herein.

175. Inasmuch as the allegations of paragraph 175 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 175 alleges facts and is

deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

176. Inasmuch as the allegations of paragraph 176 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 176 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

177. Inasmuch as the allegations of paragraph 177 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 177 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

178. Inasmuch as the allegations of paragraph 178 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 178 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

179. Inasmuch as the allegations of paragraph 179 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 179 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

180. Inasmuch as the allegations of paragraph 180 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is

required. To the extent that paragraph 180 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

*SEVENTH CAUSE OF ACTION:*

*SECTION 2 OF THE SHERMAN ACT (MONOPOLIZATION BY GENENTECH*

(Against Genentech)

181. In response to the allegations of paragraph 181 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-180 as if fully set forth herein.

182. Inasmuch as the allegations of paragraph 182 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 182 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

183. Inasmuch as the allegations of paragraph 183 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 183 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

184. Inasmuch as the allegations of paragraph 184 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 184 alleges facts and is deemed to relate to city of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

185. Inasmuch as the allegations of paragraph 185 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 185 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

*EIGHTH CAUSE OF ACTION:*

*THE CARTWRIGHT ACT*
*(UNLAWFUL RESTRAINT OF TRADE)*

(Against Genentech and Celltech)

186. In response to the allegations of paragraph 186 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-185 as if fully set forth herein.

187. Inasmuch as the allegations of paragraph 187 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 187 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

188. Inasmuch as the allegations of paragraph 188 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 188 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

189. Inasmuch as the allegations of paragraph 189 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 189 alleges facts and is

deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

190. Inasmuch as the allegations of paragraph 190 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 190 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

191. Inasmuch as the allegations of paragraph 191 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 191 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

*NINTH CAUSE OF ACTION:*

*THE CARTWRIGHT ACT*
*(CONSPIRACY TO MONOPOLIZE)*

(Against Genentech and Celltech)

192. In response to the allegations of paragraph 192 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-191 as if fully set forth herein.

193. Inasmuch as the allegations of paragraph 193 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 193 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

194. Inasmuch as the allegations of paragraph 194 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 194 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

195. Inasmuch as the allegations of paragraph 195 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 195 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

196. Inasmuch as the allegations of paragraph 196 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 196 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

197. Inasmuch as the allegations of paragraph 197 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 197 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

198. Inasmuch as the allegations of paragraph 198 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 198 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

*TENTH CAUSE OF ACTION:*

*SECTION 17200 OF THE CALIFORNIA BUSINESS & PROFESSIONS CODE*

(Against Genentech and Celltech)

199. In response to the allegations of paragraph 199 of the First Amended Complaint, City of Hope incorporates its responses in paragraphs 1-198 as if fully set forth herein.

200. Inasmuch as the allegations of paragraph 200 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 200 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

201. Inasmuch as the allegations of paragraph 201 of the First Amended Complaint do not relate to City of Hope and purport to state legal conclusions, no response thereto is required. To the extent that paragraph 201 alleges facts and is deemed to relate to City of Hope, City of Hope lacks sufficient knowledge to form a belief or understanding as to the truth of the allegations, and therefore denies them.

*PRAYER FOR RELIEF*

1. Defendant denies each and every allegation and request for relief contained in paragraph 1 of the Prayer for Relief of the First Amended Complaint.

2. Defendant denies each and every allegation and request for relief contained in paragraph 2 of the Prayer for Relief of the First Amended Complaint.

3. Defendant denies each and every allegation and request for relief contained in paragraph 3 of the Prayer for Relief of the First Amended Complaint.

4. Defendant denies each and every allegation and request for relief contained in paragraph 4 of the Prayer for Relief of the First Amended Complaint.

5. Defendant denies each and every allegation and request for relief contained in paragraph 5 of the Prayer for Relief of the First Amended Complaint.

6. Defendant denies each and every allegation and request for relief contained in paragraph 6 of the Prayer for Relief of the First Amended Complaint.

7. Defendant denies each and every allegation and request for relief contained in paragraph 7 of the Prayer for Relief of the First Amended Complaint.

8. Defendant denies each and every allegation and request for relief contained in paragraph 8 of the Prayer for Relief of the First Amended Complaint.

9. Defendant denies each and every allegation and request for relief contained in paragraph 9 of the Prayer for Relief of the First Amended Complaint.

10. Defendant denies each and every allegation and request for relief contained in paragraph 10 of the Prayer for Relief of the First Amended Complaint.

*AFFIRMATIVE DEFENSES*

As separate and distinct affirmative defenses to the causes of action set forth in the Amended Complaint, but without assuming any additional burden of proof except as may otherwise exist based on MedImmune's claims and allegations, City of Hope alleges as follows:

*FIRST AFFIRMATIVE DEFENSE*

1. The First Amended Complaint, and each and every claim set forth therein, fails to state a claim upon which relief can be granted.

*SECOND AFFIRMATIVE DEFENSE*

2. MedImmune has an adequate remedy at law and no basis exists for the grant of equitable relief.

*THIRD AFFIRMATIVE DEFENSE*

3. MedImmune's claims are barred, in whole or in part, by the Noerr-Pennington doctrine, the First Amendment, and/or related doctrines.

*FOURTH AFFIRMATIVE DEFENSE*

4. MedImmune's claims are barred, in whole or in part, for failure to mitigate damages.

*FIFTH AFFIRMATIVE DEFENSE*

5. MedImmune's claims are barred, in whole or in part, by the equitable doctrine of unclean hands.

*SIXTH AFFIRMATIVE DEFENSE*

6. MedImmune's claims are barred, in whole or in part, by the doctrines of laches, waiver and/or estoppel.

*SEVENTH AFFIRMATIVE DEFENSE*

7. MedImmune has waived the claims asserted in its First Amended Complaint.

*EIGHTH AFFIRMATIVE DEFENSE*

8. MedImmune lacks standing to bring the claims asserted in its First Amended Complaint.

*NINTH AFFIRMATIVE DEFENSE*

9. MedImmune's claims are barred, in whole or in part, by the U.S. Patent laws.

*TENTH AFFIRMATIVE DEFENSE*

10. MedImmune's claims are barred, in whole or in part, because MedImmune's claimed injury was not caused by the acts or omissions of the defendants.

*ELEVENTH AFFIRMATIVE DEFENSE*

11. MedImmune's claims are barred, in whole or in part, by the applicable statutes of limitation.

*TWELFTH AFFIRMATIVE DEFENSE*

12. MedImmune's claims are barred, in whole or in part, by the competition privilege.

*THIRTEENTH AFFIRMATIVE DEFENSE*

13. City of Hope incorporates by reference all affirmative defenses of any other defendant in this proceeding to the extent these affirmative defenses relate to City of Hope.

*FOURTEENTH AFFIRMATIVE DEFENSE*

14. City of Hope reserves its right to raise additional affirmative defenses as they become known to City of Hope. City of Hope reserves the right to amend its answer accordingly and/or to delete affirmative defenses it determines are not applicable.

*Prayer for Relief*

WHEREFORE, City of Hope requests relief as follows:

1. That MedImmune's claims be dismissed;

2. That MedImmune take nothing by reason of its First Amended Complaint;

3. That MedImmune's request for injunctive relief by [*sic*] denied;

4. For the cost of this suit, including reasonable attorney's fees; and

5. For such other and further relief as the Court may deem proper.

Dated: September 2, 2003

IRELL & MANELLA LLP
Morgan Chn (70446)
David I. Gindler (117824)
Joseph M. Lipner (155735)

By: /s/ Joseph M. Lipner
JOSEPH M. LIPNER
Attorneys for Defendant
CITY OF HOPE

*JURY DEMAND*

Defendant city of Hope hereby demands a trial by jury on all claims and issues so triable.

Dated: September 2, 2003

IRELL & MANELLA LLP
Morgan Chu (70446)
David I. Gindler (117824)
Joseph M. Lipner (155735)

By: /s/ Joseph M. Lipner
JOSEPH M. LIPNER
Attorneys for Defendant
CITY OF HOPE

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

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Case No. CV 03-02567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff*,

v.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants*.

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# CELLTECH R&D LTD.'S AMENDED ANSWER TO FIRST AMENDED COMPLAINT

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## DEMAND FOR JURY TRIAL

Defendant Celltech R&D Ltd. ("Celltech") hereby answers the First Amended Complaint of MedImmune, Inc. ("MedImmune") and alleges as follows:

### Jurisdiction and Venue

1. Celltech admits that the Complaint purports to state a claim for declaratory relief pursuant to Fed. R. Civ. P. 57 and 28 U.S.C. §§ 2201 and 2202. Celltech further admits that it filed a complaint in the United States District Court for the Northern District of California captioned *Celltech R&D Ltd. v. Genentech, Inc.*, Civ. Act. 01-3560 JCS. Celltech admits, on information and belief, that Genentech, Inc. ("Genentech") has its principal place of business in South San Francisco, California. Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments concerning the principal place of business and place of organization of City of Hope. Celltech denies all other aver-

ments of Paragraph 1, except that inasmuch as the averments of jurisdiction purport to state legal conclusions, no response thereto is required.

2. Celltech denies the averments of Paragraph 2, except that inasmuch as the averments of venue purport to state legal conclusions, no response thereto is required.

The Parties

3. Celltech admits that the Complaint purports to state claims under the cited legal theories, but denies that Plaintiff is entitled to any relief under those causes of action. Celltech denies all other averments of Paragraph 3, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

4. Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 4, and on that basis denies those averments.

5. Celltech admits that Plaintiff sells a product under the name Synagis. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 5, and on that basis denies those averments.

6. Celltech admits on information and belief that Genentech is a Delaware corporation with its principal place of business in South San Francisco, California.

7. Celltech admits that U.S. Patent No. 6,331,415 B1 states that City of Hope of Duarte, California is an assignee of the patent. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 7, and on that basis denies those averments.

8. Celltech admits that it is a British company with its principal place of business at 208 Bath Road, Slough, Berkshire, SL 1 WE, United Kingdom. Celltech admits that

the Medical Research Council granted a sub-license to MedImmune under U.S. Patent No. 4,816,397 (the "Boss Patent").

9. Celltech admits that the Complaint includes a demand for declaratory relief, but denies that Plaintiff is entitled to any such relief. Celltech denies each and every other averment set forth in Paragraph 9.

10. Celltech admits that it entered into certain agreements with Genentech to settle a patent interference relating to the Boss Patent and U.S. Patent Application No. 205,419 (the "Cabilly Application"), and to secure for Celltech a license to certain rights under U.S. Patent No. 6,331,415 B1 (the "Cabilly Patent"). Celltech further admits that the details of those agreements are confidential and proprietary. Celltech denies each and every other averment set forth in Paragraph 10.

11. Celltech admits that it entered into certain agreements with Genentech to settle a patent interference relating to the Boss Patent and the Cabilly Application, and to secure for Celltech a license to certain rights under the Cabilly Patent. Celltech further admits that it prevailed in the patent interference (Interference No. 102,572) before the PTO Board of Patent Interferences and Appeals and that Judge Maxine M. Chesney of the United States District Court for the Northern District of California denied Genentech's motion for summary judgment in the § 146 interference proceeding that was initiated by Genentech. Celltech denies each and every other averment set forth in Paragraph 11.

12. Celltech admits that, prior to March 16, 2001, it entered into certain agreements with Genentech to settle legal proceedings relating to Boss Patent and the Cabilly Application, and to secure for Celltech a license to certain rights under the Cabilly Patent. Celltech denies each and every other averment set forth in Paragraph 12.

13. Celltech admits that its 2001 Annual Report states that "Celltech has secured preferential access for its development programmes to the Cabilly patent, which covers the production of a broad range of antibody or antibody fragment products, for its 17 year life." Celltech further admits that a Celltech press release dated December 18, 2001 states: "By this settlement, Celltech will be compensated by Genentech in terms of income from sales of products which would otherwise have been covered by the Boss patent until its normal expiry date in 2006." Celltech denies each and every other averment set forth in Paragraph 13.

14. Inasmuch as the averments of Paragraph 14 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 14, and on that basis denies those averments.

15. Celltech admits that Celltech and the Medical Research Council granted several licenses to the Boss patent. Celltech further admits that the original term of the Boss patent would have expired on March 28, 2006. Celltech denies each and every other averment set forth in Paragraph 15.

16. Inasmuch as the averments of Paragraph 16 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 16, and on that basis denies those averments.

17. Celltech admits that the term of the Cabilly Patent will expire in 2018. Celltech denies each and every other averment set forth in Paragraph 17.

18. Inasmuch as the averments of Paragraph 18 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech

is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 18, and on that basis denies those averments.

19. Celltech admits that the Complaint purports to state claims under the cited statutes and legal theories, but denies that Plaintiff is entitled to any such relief. Celltech denies each and every other averment set forth in Paragraph 19.

20. Celltech admits that the Complaint demands declaratory relief, but denies that Plaintiff is entitled to any such relief. Celltech denies each and every other averment set forth in Paragraph 20.

21. Celltech admits that U.S. Patent No. 4,816,567 states that Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel filed U.S. Patent Application No. 483,457 on April 8, 1983. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 21, and on that basis denies those averments.

22. Celltech admits that U.S. Patent No. 4,816,567 states that it issued on March 28, 1989, based on U.S. Patent Application No. 483,457. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 22, and on that basis denies those averments.

23. Celltech admits that U.S. Patent No. 6,331,415 B1 states that U.S. Patent Application 07/205,419 was filed on June 10, 1988, as a continuation of U.S. Patent Application 06/483,457. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 23, and on that basis denies those averments.

24. Celltech admits that U.S. Patent No. 4,816,567 and U.S. Patent No. 4,816,397 were both issued by the PTO on March 28, 1989.

25. Celltech admits that Genentech amended its Cabilly Application and sought to provoke an interference with the Boss patent. Celltech further admits that Patent Interference No. 102,572 was declared by the PTO on February 28, 1991. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 25, and on that basis denies those averments, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

26. Celltech admits that, on February 28, 1991, the PTO Board of Patent Interferences and Appeals declared Patent Interference No. 102,572 between certain claims of the Cabilly Application and the Boss Patent. Celltech denies each and every other averment set forth in Paragraph 26, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

27. Celltech admits that Patent Interference No. 102,572 was declared on February 28, 1991 and that the final decision of the PTO Board of Patent Appeals and Interferences was issued on August 13, 1998. Celltech admits that both Celltech and Genentech made arguments to the PTO Board of Patent Appeals and Interferences relating to priority of invention. Celltech denies each and every other averment set forth in Paragraph 27.

28. Celltech admits that final decision of the PTO Board of Patent Appeals and Interferences, issued on August 13, 1998, entered judgment in favor of the Celltech inventors, and refers to that decision for its content. Celltech denies each and every other averment set forth in Paragraph 28.

29. Celltech admits that, on October 9, 1998, Genentech initiated a civil action under 35 U.S.C. § 146 entitled *Genentech, Inc. v. Celltech R&D Ltd.*, Case No. C98-3926 MMC (the "Civil Action"), in the United States District Court for the Northern District of California. Celltech denies each and every other averment set forth in Paragraph 29.

30. Celltech admits that the Civil Action was filed on October 9, 1998 and judgment was entered by the district court on March 16, 2001. Celltech admits that the Civil Action included depositions, document production, and expert disclosures. Celltech denies each and every other averment set forth in Paragraph 30.

31. Celltech admits that, during the course of the Civil Action, Genentech produced a draft Cabilly patent application. Celltech admits that Genentech made certain contentions regarding the draft Cabilly patent application, including statements made in Genentech's summary judgment papers filed in the Civil Action, and refers to Genentech's motion papers for their content. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 31, and on that basis denies those averments.

32. Celltech admits that Genentech moved in the Civil Action for summary judgment in its favor, and refers to Genentech's motion papers for their content. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 32, and on that basis denies those averments, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

33. Celltech admits that it opposed Genentech's motion for summary judgment in the Civil Action, and refers to its motion papers for their content. Celltech denies each and every other averment set forth in Paragraph 33, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

34. Celltech admits that Genentech filed a reply brief in support of its motion for summary judgment, and refers to Genentech's motion papers for their content. Celltech admits that Genentech filed a motion for summary judgment that

Celltech was not entitled to priority to the March 25, 1983 filing date of the United Kingdom Boss patent application, and refers to Genentech's motion papers for their content. Celltech denies each and every other averment set forth in Paragraph 34.

35. Celltech admits that summary judgment motions were filed in the Civil Action, and refers to the papers filed by the parties for their content. Celltech denies each and every other averment set forth in Paragraph 35, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

36. Celltech admits that it entered into certain agreements with Genentech to settle a patent interference relating to the Boss Patent and the Cabilly Application, and to secure for Celltech a license to certain rights under the Cabilly Patent. Celltech further admits that it prevailed in the patent interference before the PTO Board of Patent Interferences and Appeals and that Judge Maxine M. Chesney of the United States District Court for the Northern District of California denied Genentech's motion for summary judgment in the § 146 interference proceeding that was initiated by Genentech. Celltech denies each and every other averment set forth in Paragraph 36.

37. Celltech denies each and every averment set forth in Paragraph 37, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

38. Celltech denies each and every averment set forth in Paragraph 38, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

39. Celltech admits that in connection with their settlement agreement, Genentech and Celltech submitted a proposed order to the District Court, and that the proposed order contained several proposed findings of fact and conclusions of law, including a proposed finding that "Genentech is

entitled as a matter of law to priority over Celltech to invention described by the count." Celltech denies each and every other averment set forth in Paragraph 39, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

40. Celltech denies each and every averment set forth in Paragraph 40, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

41. Celltech admits that the District Court executed the proposed order and entered that Order on March 16, 2001, and refers to the Order for its content. Celltech denies each and every other averment set forth in Paragraph 41.

42. Celltech admits the District Court entered a Judgment in the Civil Action, and refers to the Judgment for is content. Celltech further admits that, among other things, the District Court's Judgment directed the PTO to: "vacate the PTO's decision in *Cabilly et al. v. Boss et al.*, Patent Interference No. 102,572"; "revoke and vacate United States Patent No. 4,816,397, issued March 28, 1989 to Boss *et al.*"; and "grant and issue to Genentech's Inventors (with Genentech as the assignee), with the issue date being the same as the date of revocation of United States Patent No. 4,816,397, a United States patent . . . ." Celltech denies each and every other averment set forth in paragraph 42.

43. Celltech admits that, following entry of the District Court's Judgment, the PTO Board of Patent Interferences and Appeals issued a Final Order After District Court Judgment, and refers to the Final Order for its terms. Celltech denies each and every other averment set forth in Paragraph 43.

44. Celltech denies each and every averment set forth in Paragraph 44.

45. Celltech admits that the PTO Board of Patent Interferences and Appeals' Final Order After District Court Judg-

ment stated, in part, "[w]e will note that if a patent is issued to Cabilly, its term will begin to run now and the public has already been subject to patent rights of Boss since 1989, and that the interference has been pending since 1991." Celltech refers to the Final Order for its terms. Celltech denies each and every other averment set forth in Paragraph 45.

46. Celltech admits that the PTO Board of Patent Interferences and Appeals issued a Final Order After District Court Judgment, and refers to the Final Order for its terms. Celltech denies each and every other averment set forth in Paragraph 46.

47. Celltech admits that it commenced a civil action, *Celltech R&D Ltd. v. Genentech, Inc.*, in the United States District Court for the Northern District of California pursuant to 35 U.S.C. § 146. Celltech denies each and every other averment set forth in Paragraph 47.

48. Inasmuch as the averments of Paragraph 48 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits the PTO Board of Patent Interferences and Appeals referred the Cabilly Application to a patent examiner. Celltech denies each and every other averment set forth in Paragraph 48.

49. Inasmuch as the averments of Paragraph 49 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 49, and on that basis denies those averments.

50. Inasmuch as the averments of Paragraph 50 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 50, and on that basis denies those averments.

51. Inasmuch as the averments of Paragraph 51 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 51, and on that basis denies those averments.

52. Inasmuch as the averments of Paragraph 52 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 52, and on that basis denies those averments.

53. Inasmuch as the averments of Paragraph 53 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that it presented expert evidence during the Civil Action and that it opposed Genentech's motions for summary judgment. Celltech refers to the papers filed by Celltech for their content. Celltech denies each and every other averment set forth in Paragraph 53.

54. Inasmuch as the averments of Paragraph 54 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that it submitted an expert report by Dr. Jonathan S. Weissman and refers to the report for its content. Celltech denies each and every other averment set forth in Paragraph 54.

55. Inasmuch as the averments of Paragraph 55 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech referenced a draft Cabilly patent application in its summary judgment briefing regarding priority. Celltech further admits that a draft Cabilly patent application is referenced in the March-16, 2001 Order Re-

garding Resolution of Interference. Celltech refers to the draft Cabilly patent application for its content Celltech is without knowledge or information sufficient to form a belief as to the truth of the remaining averments in Paragraph 55, and on that basis denies those averments.

56. Inasmuch as the averments of Paragraph 56 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 56, and on that basis denies those averments.

57. Inasmuch as the averments of Paragraph 57 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech responded to the arguments raised in Celltech's opposition to Genentech's motion for summary judgment. Celltech refers to the papers filed by Genentech for their content. Celltech denies the remaining allegations of Paragraph 57.

58. Inasmuch as the averments of Paragraph 58 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech moved for summary judgment regarding the Celltech British Application. Celltech refers to the papers filed by Genentech for their content. Celltech denies the remaining allegations of Paragraph 58.

59. Inasmuch as the averments of Paragraph 59 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that during the Civil Action, counsel for Genentech took the deposition of Celltech's expert Dr. Weissman. Celltech refers to the deposition transcript for its content. Celltech denies the remaining allegations of Paragraph 59.

60. Inasmuch as the averments of Paragraph 60 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech moved for summary judgment regarding the Celltech British Application. Celltech refers to the papers filed by Genentech for their content. Celltech denies the remaining allegations of Paragraph 60.

61. Inasmuch as the averments of Paragraph 61 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech moved for summary judgment during the Civil Action. Celltech refers to the papers filed by Genentech for their content. Celltech denies the remaining allegations of Paragraph 61.

62. Inasmuch as the averments of Paragraph 62 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech moved for summary judgment during the Civil Action. Celltech refers to the papers filed by Genentech for their content. Celltech denies the remaining allegations of Paragraph 62.

63. Inasmuch as the averments of Paragraph 63 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 63, and on that basis denies those averments.

64. Inasmuch as the averments of Paragraph 64 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech denies each and every averment set forth in Paragraph 64.

65. Inasmuch as the averments of Paragraph 65 do not relate to Celltech, no response thereto is required. To the

extent this Paragraph is deemed to relate to Celltech, Celltech denies each and every averment set forth in Paragraph 65.

66. Inasmuch as the averments of Paragraph 66 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that it entered into certain agreements with Genentech to settle the Civil Action. Celltech denies each and every other averment set forth in Paragraph 66.

67. Inasmuch as the averments of Paragraph 67 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 67, and on that basis denies those averments.

68. Inasmuch as the averments of Paragraph 68 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 68, and on that basis denies those averments.

69. Inasmuch as the averments of Paragraph 69 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 69, and on that basis denies those averments.

70. Inasmuch as the averments of Paragraph 70 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 70, and on that basis denies those averments.

71. Inasmuch as the averments of Paragraph 71 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 71, and on that basis denies those averments.

72. Inasmuch as the averments of Paragraph 72 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 72, and on that basis denies those averments.

73. Inasmuch as the averments of Paragaph 73 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 73, and on that basis denies those averments.

74. Inasmuch as the averments of Paragraph 74 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 74, and on that basis denies those averments.

75. Inasmuch as the averments of Paragraph 75 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 75, and on that basis denies those averments.

76. Inasmuch as the averments of Paragraph 76 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 76, and on that basis denies those averments.

77. Inasmuch as the averments of Paragraph 77 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 77, and on that basis denies those averments.

78. Inasmuch as the averments of Paragraph 78 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 78, and on that basis denies those averments.

79. Inasmuch as the averments of Paragraph 79 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 79, and on that basis denies those averments.

80. Inasmuch as the averments of Paragraph 80 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech submitted an Information Disclosure Statement on September 18, 1991 and refers to that document for its content. Celltech denies the remaining allegations of Paragraph 80.

81. Inasmuch as the averments of Paragraph 81 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech submitted an Information Disclosure Statement on September 18, 1991 and refers to that document for its content. Celltech denies the remaining allegations of Paragraph 81.

82. Inasmuch as the averments of Paragraph 82 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech filed a Notice of Opposition with the European Patent Office regarding the European Boss Patent. Celltech refers to those documents for their contents. Celltech denies the remaining allegations of Paragraph 82.

83. Inasmuch as the averments of Paragraph 83 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech filed a Notice of Opposition with the European Patent Office regarding the European Boss Patent. Celltech refers to that document for its contents. Celltech denies the remaining allegations of Paragraph 83.

84. Inasmuch as the averments of Paragraph 84 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that Genentech filed a Notice of Opposition with the European Patent Office regarding the European Boss Patent. Celltech refers to that document for its contents. Celltech denies the remaining allegations of Paragraph 84.

85. Inasmuch as the averments of Paragraph 85 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 85, and on that basis denies those averments.

86. Inasmuch as the averments of Paragraph 86 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 86, and on that basis denies those averments.

87. Inasmuch as the averments of Paragraph 87 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Board issued an order dated July 25, 2001 and refers to the order for its content. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 87, and on that basis denies those averments.

88. Inasmuch as the averments of Paragraph 88 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 88, and on that basis denies those averments.

89. Inasmuch as the averments of Paragraph 89 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 89, and on that basis denies those averments.

90. Inasmuch as the averments of Paragraph 90 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge

or information sufficient to form a belief as to the truth of the averments in Paragraph 90, and on that basis denies those averments.

91. Inasmuch as the averments of Paragraph 91 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 91, and on that basis denies those averments.

92. Inasmuch as the averments of Paragraph 92 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 92, and on that basis denies those averments.

93. Inasmuch as the averments of Paragraph 93 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 93, and on that basis denies those averments.

94. Inasmuch as the averments of Paragraph 94 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 94, and on that basis denies those averments.

95. Inasmuch as the averments of Paragraph 95 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 95, and on that basis denies those averments.

96. Inasmuch as the averments of Paragraph 96 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 96, and on that basis denies those averments.

97. Inasmuch as the averments of Paragraph 97 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech refers to the Stanford Application for its content, and Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 97, and on that basis denies those averments.

98. Inasmuch as the averments of Paragraph 98 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 98, and on that basis denies those averments.

99. Inasmuch as the averments of Paragraph 99 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 99, and on that basis denies those averments.

100. Inasmuch as the averments of Paragraph 100 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 100, and on that basis denies those averments.

101. Inasmuch as the averments of Paragraph 101 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech refers to the Axel patents for their contents, and Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 101, and on that basis denies those averments.

102. Inasmuch as the averments of Paragraph 102 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 102, and on that basis denies those averments.

103. Inasmuch as the averments of Paragraph 103 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 103, and on that basis denies those averments.

104. Inasmuch as the averments of Paragraph 104 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 104, and on that basis denies those averments.

105. Inasmuch as the averments of Paragraph 105 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech refers to the Axel patents for their contents, and Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 105, and on that basis denies those averments.

106. Inasmuch as the averments of Paragraph 106 purport to state legal conclusions and do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 106, and on that basis denies those averments.

107. Inasmuch as the averments of Paragraph 107 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that U.S. Patent No. 6,331,415 B1, issued on December 18, 2001. Celltech is without knowledge or information sufficient to form a belief as to the truth of every other averment in Paragraph 107, and on that basis denies those averments.

108. Inasmuch as the averments of Paragraph 108 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that U.S. Patent No. 6,331,415 B1 is titled "Method of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein," and lists Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel as inventors. Celltech further admits that the patent lists Genentech as the assignee and that a Certificate of Correction issued by the PTO on June 25, 2002 added City of Hope as an additional assignee. Celltech is without knowledge or information sufficient to form a belief as to the truth of every other averment in Paragraph 108, and on that basis denies those averments.

109. Inasmuch as the averments of Paragraph 109 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech. Celltech admits that certain antibody molecules can be used to provide beneficial treatment for certain illnesses. Celltech is without knowledge or information sufficient to form a belief as to the

truth of every other averment in Paragraph 109, and on that basis denies those averments.

110. Celltech admits that it issued a press release on December 18, 2001, denies that MedImmune has accurately quoted the press release, and refers to the press release for its terms. Celltech further admits that the press release stated, in part, that "By this settlement, Celltech will be compensated by Genentech in terms of income from sales of products which would otherwise have been covered by the Boss Patent until its normal expiry date in 2006." Celltech denies each and every other averment set forth in Paragraph 110.

111. Celltech admits that it issued a press release on December 18, 2001, denies that MedImmune has accurately quoted the press release, and refers to the press release for its terms. Celltech further admits that the press release stated, in part, that "Celltech has also secured rights to Genentech's Cabilly patent for its products." Celltech denies each and every other averment set forth in Paragraph 111.

112. Celltech admits the referenced Senate Report contains the quoted language. Celltech further admits that Celltech and Genentech filed their settlement agreement with the PTO under seal pursuant to applicable PTO rules and procedures. Celltech denies each and every other averment of Paragraph 112, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

113. Inasmuch as the averments of Paragraph 113 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 113, and on that basis denies those averments.

114. Inasmuch as the averments of Paragraph 114 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech

is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 114, and on that basis denies those averments.

115. Celltech admits that, on May 8, 2002, Plaintiff petitioned the PTO for access to Celltech's and Genentech's settlement agreement, and that Celltech and Genentech opposed that petition pursuant to applicable rules of the PTO. Celltech further states that, on April 4, 2003, the PTO Board of Patent Interferences and Appeals rejected Plaintiff's petition, finding that the petition "appears to constitute a 'fishing expedition' that cannot be granted absent, as respondents have indicated, 'something more' constituting the requisite 'good cause.'" Celltech denies each and every other averment set forth in Paragraph 115.

116. Inasmuch as the averments of Paragraph 116 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 116, and on that basis denies those averments.

117. Inasmuch as the averments of Paragraph 117 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 117, and on that basis denies those averments.

118. Inasmuch as the averments of Paragraph 118 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 118, and on that basis denies those averments.

119. Inasmuch as the averments of Paragraph 119 do not relate to Celltech, no response thereto is required. To the

extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 119, and on that basis denies those averments.

120. Celltech denies each and every averment set forth in Paragraph 120.

121. Celltech admits that it owned the Boss patent. Celltech further admits that it granted to the Medical Research Council in London a license to the Boss patent, which license included the right to grant sublicenses, and refers to the sublicenses granted by Medical Research Council for their terms. Celltech denies each and every other averment set forth in Paragraph 121.

122. Celltech admits that Plaintiff, as well as several other individuals and entities, obtained a sublicense to the Boss patent. Celltech denies each and every other averment set forth in Paragraph 122.

123. Celltech denies each and every averment set forth in Paragraph 123.

124. Inasmuch as the averments of Paragraph 124 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 124, and on that basis denies those averments.

125. Inasmuch as the averments of Paragraph 125 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 125, and on that basis denies those averments.

126. Inasmuch as the averments of Paragraph 126 purport to state legal conclusions, no response thereto is required. To

the extent a response is required, Celltech denies each and every averment set forth in Paragraph 126.

127. Inasmuch as the averments of Paragraph 127 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 127, and on that basis denies those averments.

128. Inasmuch as the averments of Paragraph 128 purport to state legal conclusions, no response thereto is required. To the extent a response is required, Celltech denies each and every averment set forth in Paragraph 128.

129. Celltech denies that it engaged in unlawful conduct. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 129, and on that basis denies those averments.

130. Celltech denies that it engaged in unlawful conduct. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 130, and on that basis denies those averments.

First Cause of Action
Declaratory Judgment on Contractual Rights and Obligations
(Against Genentech)

131. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 130 of this Answer as if fully set forth herein.

132. Inasmuch as the averments of Paragraph 132 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 132, and on that basis denies those averments.

133. Inasmuch as the averments of paragraph 133 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Complaint purports to state a claim for declaratory judgment. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 133, and on that basis denies those averments.

Second Cause of Action
Patent Invalidity
(Against Genentech and City of Hope)

134. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 133 of this Answer as if fully set forth herein.

135. Inasmuch as the averments of Paragraph 135 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 135, and on that basis denies those averments.

136. Inasmuch as the averments of Paragraph 136 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 136, and on that basis denies those averments.

137. Inasmuch as the averments of Paragraph 137 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief

as to the truth of the averments in Paragraph 137, and on that basis denies those averments.

138. Inasmuch as the averments of Paragraph 138 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 138, and on that basis denies those averments.

139. Inasmuch as the averments of Paragraph 139 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Complaint purports to state a claim for declaratory judgment. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 139, and on that basis denies those averments.

Third Cause of Action
Patent Unenforceability
(Against Genentech and City of Hope)

140. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 139 of this Answer as if fully set forth herein.

141. Inasmuch as the averments of Paragraph 141 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 141, and on that basis denies those averments.

142. Inasmuch as the averments of Paragraph 142 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph

avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 142, and on that basis denies those averments.

143. Inasmuch as the averments of Paragraph 143 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 143, and on that basis denies those averments.

144. Celltech incorporates and restates its answers to the averments contained in Paragraphs 48 through 106 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 144 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 144, and on that basis denies those averments.

145. Celltech incorporates and restates its answers to the averments contained in Paragraphs 52 through 78 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 145 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 145, and on that basis denies those averments.

146. Celltech incorporates and restates its answers to the averments contained in Paragraphs 52 through 78 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 146 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the

extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 146, and on that basis denies those averments.

147. Inasmuch as the averments of Paragraph 147 do not relate to Celltech, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 147, and on that basis denies those averments.

148. Celltech incorporates and restates its answers to the averments contained in Paragraphs 66 and 76-77 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 148 do not relate to Celltech, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 148, and on that basis denies those averments.

149. Celltech incorporates and restates its answers to the averments contained in Paragraphs 79-91 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 149 do not relate to Celltech, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 149, and on that basis denies those averments.

150. Celltech incorporates and restates its answers to the averments contained in Paragraphs 79-91 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 150 do not relate to Celltech, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or informa-

tion sufficient to form a belief as to the truth of the averments in Paragraph 150, and on that basis denies those averments.

151. Celltech incorporates and restates its answers to the averments contained in Paragraphs 92-99 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 151 do not relate to Celltech, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 151, and on that basis denies those averments.

152. Celltech incorporates and restates its answers to the averments contained in Paragraphs 92-99 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 152 do not relate to Celltech, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 152, and on that basis denies those averments.

153. Celltech incorporates and restates its answers to the averments contained in Paragraphs 100-106 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 153 do not relate to Celltech, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 153, and on that basis denies those averments.

154. Celltech incorporates and restates its answers to the averments contained in Paragraphs 100-106 of this Answer as if fully set forth herein. Inasmuch as the averments of Paragraph 154 do not relate to Celltech, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the

averments in Paragraph 154, and on that basis denies those averments.

155. Inasmuch as the averments of Paragraph 155 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments a Paragraph 155, and on that basis denies those averments.

156. Inasmuch as the averments of Paragraph 156 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 156, and on that basis denies those averments.

157. Inasmuch as the averments of Paragraph 157 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 157, and on that basis denies those averments.

158. Inasmuch as the averments of Paragraph 158 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 158, and on that basis denies those averments.

159. Inasmuch as the averments of Paragraph 159 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 159, and on that basis denies those averments.

160. Inasmuch as the averments of Paragraph 160 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 160, and on that basis denies those averments.

161. Inasmuch as the averments of Paragraph 161 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Complaint purports to state a claim for declaratory judgment. Celltech is without knowledge or information sufficient to form a belief as to the truth of the other averments in Paragraph 161, and on that basis denies those averments.

Fourth Cause of Action
Non-Infringement
(Against Genentech and City of Hope)

162. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 161 of this Answer as if fully set forth herein.

163. Inasmuch as the averments of Paragraph 163 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 163, and on that basis denies those averments.

164. Inasmuch as the averments of Paragraph 164 do not relate to Celltech, no response thereto is required. To the extent this Paragraph is deemed to relate to Celltech, Celltech admits that the Complaint purports to state a claim for declaratory judgment. Celltech is without knowledge or information sufficient to form a belief as to the truth of the

other averments in Paragraph 164, and on that basis denies those averments.

Fifth Cause of Action
Section 1 of the Sherman Act
(Against Genentech and Celltech)

165. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 164 of this Answer as if fully set forth herein.

166. Celltech denies each and every averment set forth in Paragraph 166.

167. Celltech denies each and every averment set forth in Paragraph 167.

168. Celltech denies each and every averment set forth in Paragraph 168, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

169. Celltech denies each and every averment set forth in Paragraph 169.

170. Celltech denies each and every averment set forth in Paragraph 170, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

171. Celltech denies each and every averment set forth in Paragraph 171, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

172. Celltech denies each and every averment set forth in Paragraph 172, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

173. Celltech denies that Plaintiff is entitled to any relief under Section 1 of the Sherman Act and denies each and every other averment set forth in Paragraph 173, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Sixth Cause of Action
Section 2 of the Sherman Act (Conspiracy to Monopolize)
(Against Genentech and Celltech)

174. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 173 of this Answer as if fully set forth herein.

175. Celltech denies each and every averment set forth in Paragraph 175.

176. Celltech denies each and every averment set forth in Paragraph 176.

177. Celltech denies each and every averment set forth in Paragraph 177, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

178. Celltech denies each and every averment set forth in Paragraph 178.

179. Celltech denies each and every averment set forth n Paragraph 179 except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

180. Celltech denies that Plaintiff is entitled to any relief under Section 2 of the Sherman Act and denies each and every averment set forth in Paragraph 180, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Seventh Cause of Action
Section 2 of the Sherman Act
(Against Genentech)

181. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 180 of this Answer as if fully set forth herein.

182. Inasmuch as the averments of Paragraph 182 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph

avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 182, and on that basis denies those averments.

183. Inasmuch as the averments of Paragraph 183 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 183, and on that basis denies those averments.

184. Inasmuch as the averments of Paragraph 184 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 184, and on that basis denies those averments.

185. Inasmuch as the averments of Paragraph 185 do not relate to Celltech and purport to state legal conclusions, no response thereto is required. To the extent this Paragraph avers facts and is deemed to relate to Celltech, Celltech is without knowledge or information sufficient to form a belief as to the truth of the averments in Paragraph 185, and on that basis denies those averments.

Eighth Cause of Action
The Cartwright Act (Unlawful Restraint of Trade)
(Against Genentech and Celltech)

186. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 185 of this Answer as if fully set forth herein.

187. Celltech denies each and every averment set forth in Paragraph 187.

188. Celltech denies each and every averment set forth in Paragraph 188.

189. Celltech denies each and every averment set forth in Paragraph 189, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

190. Celltech denies each and every averment set forth in Paragraph 190, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

191. Celltech denies that Plaintiff is entitled to any relief under the Cartwright Act and denies each and every other averment set forth in Paragraph 191, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required

Ninth Cause of Action
The Cartwright Act (Conspiracy to Monopolize)
(Against Genentech and Celltech)

192. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 191 of this Answer as if fully set forth herein.

193. Celltech denies each and every averment set forth in Paragraph 193.

194. Celltech denies each and every averment set forth in Paragraph 194.

195. Celltech denies each and every averment set forth in Paragraph 195, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

196. Celltech denies each and every averment set forth in Paragraph 196.

197. Celltech denies each and every averment set forth in Paragraph 197, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

198. Celltech denies that Plaintiff is entitled to any relief under the Cartwright Act and denies each and every averment set forth in Paragraph 198, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Tenth Cause of Action
Section 17200 of the California Business & Professions Code
(Against Genentech and Celltech)

199. Celltech incorporates and restates its answers to the averments contained in Paragraphs 1 through 198 of this Answer as if fully set forth herein.

200. Celltech denies each and every averment set forth in Paragraph 200, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

201. Celltech denies that Plaintiff is entitled any relief under Section 17200 and denies each and every averment set forth in Paragraph 201, except that inasmuch as the averments purport to state legal conclusions, no response thereto is required.

Affirmative Defenses

As for its further and separate defenses, Celltech states the following affirmative defenses without assuming the burden of proof on such defenses that would otherwise rest on Plaintiff.

First Affirmative Defense

202. The causes of action asserted in the Complaint fail to state a claim upon which relief may be granted.

Second Affirmative Defense

203. Plaintiff has an adequate remedy at law and no basis exists for the grant of equitable relief.

Third Affirmative Defense

204. Plaintiff's causes of action are barred by the *Noerr-Pennington* doctrine, the First Amendment and/or related doctrines.

Fourth Affirmative Defense

205. Plaintiff's claims are barred for failure to mitigate damages.

Fifth Affirmative Defense

206. Plaintiff's claims are barred to the extent that Plaintiff's purported injuries and damages were not proximately caused by any acts or omissions of Celltech.

Sixth Affirmative Defense

207. The Fifth, Sixth, Eighth, Ninth, and Tenth causes of action should be dismissed because Plaintiff has not suffered, and will not suffer, injury of the type the antitrust laws were designed to prevent.

Seventh Affirmative Defense

208. The equitable doctrine of unclean hands prevents the relief requested by Plaintiff.

Eighth Affirmative Defense

209. Any and all of Celltech's conduct challenged by Plaintiff was justified, constituted bona fide business competition, and was carried out in furtherance of Celltech's legitimate business objectives.

Ninth Affirmative Defense

210. The Fifth, Sixth, Eighth, Ninth, and Tenth causes of action are barred by the U.S. patent laws.

Tenth Affirmative Defense

211. Plaintiff's causes of action are barred by the equitable doctrines of waiver, laches, and estoppel.

Eleventh Affirmative Defense

212. Plaintiff lacks standing to the bring causes of action asserted in the Complaint.

Twelfth Affirmative Defense

213. Celltech hereby adopts and incorporates by reference all other affirmative defenses asserted by any other defendant in this proceeding to the extent these affirmative defenses relate to Celltech.

Prayer for Relief

WHEREFORE, Celltech requests relief as follows:

1. That Plaintiffs claims be dismissed;

2. That Plaintiff take nothing by reason of its Complaint for Damages;

3. That Plaintiff's request for injunctive relief be denied;

4. For the cost of this suit, including reasonable attorneys' fees; and

5. For such other and further relief as the Court may deem proper.

Demand for Jury Trial

Celltech hereby demands a trial by jury for all issues so triable in this action.

Dated: September 22, 2003

CHARLES S. BARQUIST
LORI A. SCHECHTER
STEVEN M. HAINES
JASON A. CROTTY
CHRISTOPHER P. WILLARD
MORRISON & FOERSTER LLP

By: _____
Charles S. Barquist
Attorney for Defendant
CELLTECH R&D LTD.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

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Case No. CV 03-02567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC., CITY OF HOPE, AND CELLTECH R&D LTD.,

*Defendants.*

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# CELLTECH R&D LTD'S MOTION FOR JUDGMENT ON THE PLEADINGS

## I. INTRODUCTION

MedImmune claims injuries under federal and state antitrust laws arising from the issuance of a U.S. patent to Genentech—and MedImmune's decision to license the patent rather than face infringement litigation—because the U.S. Patent and Trademark Office ("PTO") issued that patent only after Celltech and Genentech settled their litigation over which of them was the first inventor of the technology. In settling their priority litigation, Celltech and Genentech jointly sought an order from the U.S. District Court in San Francisco, and Genentech thereafter sought issuance of the patent from the PTO. However, the actions of Celltech and Genentech are immune under the *Noerr-Pennington* doctrine, which constitutionally immunizes petitioning the government, including courts and administrative agencies. The *Noerr-Pennington* doctrine bars MedImmune's claims under both federal and state law. The "sham" exception to *Noerr-Pennington* was not even alleged by MedImmune and is inapplicable in any event. The pleadings plainly demonstrate

that the actions complained of are those of a U.S. District Judge and the PTO, not Celltech or Genentech. Taking the allegations of the Complaint as true, Celltech is entitled to judgment on the pleadings on MedImmune's antitrust and unfair competition claims.

* * * *

## V. CONCLUSION

For the reasons set forth above, MedImmune's federal antitrust claims (Counts 5 and 6), state law antitrust claims (Counts 8 and 9) and state law unfair competition claim (Count 10) fail as a matter of law and Celltech is entitled to judgment on the pleadings on those counts. The actions complained of are immune from liability because they are constitutionally protected petitioning immunized by the *Noerr-Pennington* doctrine.

Dated: September 29, 2003

CHARLES S. BARQUIST
LORI A. SCHECHTER
STEVEN M. HAINES
JASON A. CROTTY
CHRISTOPHER P. WILLARD
MORRISON & FOERSTER LLP

By: /s/ Steven M. Haines
STEVEN M. HAINES

Attorneys for Defendant
CELLTECH R&D LTD.

News
Release

[Logo]
CELLTECH

For immediate release

18th December 2001

## CELLTECH AND GENENTECH SETTLE BOSS/CABILLY US PATENT INTERFERENCE

Celltech and Genentech have reached a settlement in the matter of the US Patent Office interference involving Celltech's 'Boss' patent application and Genentech's 'Cabilly' patent application, both of which relate to antibody manufacturing technology.

The settlement was concluded as a result of a mediation process ordered by the US District Court of the Northern District of California. Arising from this process, the settlement comes into effect following the recent grant of the Cabilly patent by the US Patent Office and an Order of the Court to revoke and withdraw the Boss patent and grant and issue the Cabilly patent.

By this settlement, Celltech will be compensated by Genentech in terms of income from sales of products which would otherwise have been covered by the Boss patent until its normal expiry date in 2006. Celltech has also secured rights to Genentech's Cabilly patent for its products.

Contacts:


| | | |
|---|---|---|
| Peter Allen | Chief Financial Officer | (44) (0) 1753 534655 |
| Richard Bungay | Director of Corporate Communications & Strategic Planning | |
| Jon Coles | Brunswick (London) | (44) (0) 207 404 5959 |
| Cindy Leggett-Flynn | Brunswick (New York) | (1) (212) 333 3810 |

Website: www.celltechgroup.com

Celltech Group plc (NYSE: CELL; LSE: CCH) is one of Europe's largest biopharmaceutical companies, with an extensive late stage development pipeline and a profitable cash-generative pharmaceutical business. Cellech also possesses drug discovery capabilities of exceptional strength, including a leading position in antibody engineering.

Celltech desires to take advantage of the "Safe Harbor" provisions of the US Private Securities Litigation Reform Act of 1995, with respect to forward looking statements contained within this document. In particular certain statements with regard to the future income receivable and rights granted under the terms of the agreement with Genentech are forward looking in nature. By their nature forward looking statements involve risks and uncertainties that could cause actual results to differ materially from those expressed or implied by the forward looking statements. Other factors that could affect these forward-looking statements are described in the Company's reports filed with the U.S. Securities and Exchange Commission. The forward looking statements included in this document represent the Company's best judgment as of the date hereof based in part on preliminary information and certain assumptions which management believes to be reasonable. The Company disclaims any obligation to update these forward looking statements.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

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Case No. CV03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

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# GENENTECH, INC.'S NOTICE OF MOTION AND MOTION FOR SUMMARY JUDGMENT ON PLAINTIFF'S ANTITRUST CLAIMS; MEMORANDUM IN SUPPORT

## NOTICE OF MOTION AND MOTION

PLEASE TAKE NOTICE THAT at 10:00 a.m. on December 15, 2003, or as soon thereafter as the matter can be heard, before the Honorable Mariana R. Pfaelzer, in courtroom 12 of the United States District Court for the Central District if California, defendant Genentech, Inc. ("Genentech") will and hereby does move this Court pursuant to Rule 56 of the Federal Rules of Civil Procedurefor an order granting summary judgment on plaintiff MedImmune, Inc.'s Fifth, Sixth, Seventh, Eighth, Ninth, and Tenth causes of action. Genentech's motion is made on the grounds that MedImmune, Inc.'s alleged injury was caused by governmental action, namely the issuance of U.S. Patent No. 6,311,415B1, and therefore, Genentech is immune from antitrust liability under the *Noerr-Pennington* doctrine and also because MedImmune, Inc. has not suffered antitrust injury.

This motion is based on this Notice of Motion and Motion, on the Memorandum filed concurrently herewith, on the accompanying declarations of Vernon M. Winters, Sharon E. Crane, and Christopher S. Yates, all pleadings and papers on file in this action, and on the oral argument at the hearing on the motion.

This motion is made following the conference of counsel pursuant to Local Rule 7-3 which took place on October 10, 2003. This motion is made in accordance with the Stipulation and Order Regarding Briefing and Hearing Schedule filed October 23, 2003, a copy of which is attached hereto as Exhibit 1.

Date: October 30, 2003 Respectfully submitted,

LATHAM & WATKINS LLP
Daniel M. Wall
Mark A. Flagel
Dean G. Dunlavey
Christopher S. Yates
James K. Lynch

By Daniel M. Wall
DANIEL M. WALL
Attorneys for Defendant
Genentech, Inc.

[Exhibit omitted in printing.]

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

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Case No. CV 03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D Ltd.,

*Defendants.*

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# DECLARATION OF VERNON M. WINTERS

I, Vernon M. Winters, declare:

1. I am an attorney admitted to practice law in California and am a partner with the law firm Weil, Gotshal & Manges LLP. I have personal and firsthand knowledge of the facts stated in this declaration. If called upon to do so, I could and would testify competently thereto.

2. I was previously a partner with the law firm Latham & Watkins LLP and represented Genentech in *Genentech, Inc. v. Celltech Therapeutics, Ltd.*, Docket No. C98-3926 MMC (N.D. Cal) (the "146 Action").

3. I know from my representation of Genentech in the 146 Action that Genentech commenced the 146 Action on October 9, 1998. Attached hereto as Exhibit 1 is a true and correct copy of Genentech's Complaint in the 146 Action.

4. During the course of the 146 Action, I received and produced to Celltech a copy of a draft patent application dated February 25, 1983. Attached hereto as Exhibit 2 is a true and correct copy of that draft patent application as it was produced in the 146 Action. Attached hereto as Exhibit 3 is a true and correct copy of excerpts from the deposition of Dr.

Shmuel Cabilly taken in the 146 Action, including testimony concerning the February 25, 1983 draft patent application.

5. Attached hereto as Exhibit 4 is a true and correct copy of excerpts of the deposition of Dr. Kate Murashige taken in the 146 Action, including testimony concerning the February 25, 1983 draft patent application and a further draft patent application dated March 25, 1983. Attached hereto as Exhibit 5 is a true and correct copy of a declaration provided by Dr. Murashige during the 146 Action.

6. Attached hereto as Exhibit 6 is a true and correct copy of excerpts of the deposition of Dr. Herbert Heyneker taken in the 146 Action.

7. Attached hereto as Exhibit 7 is a true and correct copy of excerpts of the deposition of Dr. Arthur Riggs taken in the 146 Action.

8. Attached hereto as Exhibit 8 is a true and correct copy of excerpts of the deposition of Dr. Ronald Wetzel taken in the 146 Action.

9. Attached hereto as Exhibits 9-11 are true and correct copies of Genentech's memorandum in support of its motion for summary adjudication regarding conception in the 146 Action. Celltech's brief in opposition to that motion, and Genentech's reply brief in support of its motion. Celltech did not move for summary judgment or summary adjudication in the 146 Action.

10. On behalf of Genentech, I attended the July 28, 2000 hearing before the Honorable Maxine M. Chesney, United States District Judge, concerning Genentech's motions for summary adjudication. Attached hereto as Exhibit 12 is a true and correct copy of the transcript of that hearing.

11. After the July 28, 2000 hearing, Genentech and Celltech agreed to mediate the dispute before the Honorable William Cahill, a retired California Superior Court Judge who

was affiliated at the time with the mediation and arbitration service, JAMS.

12. On September 15, 2000, I participated in a mediation session with Judge Cahill. Thereafter, I participated in numerous discussions with counsel for Celltech concerning settlement and concerning settlement documents. In early 2001, the parties reached agreement on a settlement. Attached hereto as Exhibit 13 is a true and correct copy of "Settlement Agreement between Genentech, Inc. and Celltech Chiroscience Limited," dated March 2, 2001. Attached hereto as Exhibit 14 is a true and correct copy of "Amended and Restated License Agreement between Genentech, Inc. and Celltech Chiroscience Limited."

13. After Genentech and Celltech had executed the Settlement Agreement and the Amended and Restated License Agreement, I worked with counsel for Celltech to inform the Court of the settlement and to prepare documents for filing with the Court. Attached hereto as Exhibit 15 is a true and correct copy of a document entitled "Notice of Settlement and Joint Request for Entry of Settlement Instruments," filed on March 6, 2001. Attached hereto as Exhibit 16 is a true and correct copy of a proposed "Order Regarding Resolution of Interference," filed March 6, 2001. Attached hereto as Exhibit 17 is a true and correct copy of a proposed "Judgment" filed March 6, 2001. Attached hereto as Exhibits 18-19 are true and correct copies of a "Proposed Order Regarding Resolution of Interference" and a "Proposed Judgment" which were filed by the Court on March 16, 2001.

14. Attached hereto as Exhibit 20 is a true and correct copy of Genentech's memorandum in support of its motion for summary adjudication regarding diligence in the 146 Action.

15. Attached hereto as Exhibit 21 is a true and correct copy of "Civil Minutes" filed March 8, 2001 from the 146 Action.

Executed this 29th day of October, 2003, at San Francisco, California.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

/s/ Vernon M. Winters
VERNON M. WINTERS

[*Exhibit 1 to Winters Declaration*]

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

[Filed Oct. 9, 1998]

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Case No. C 98-3926 CRB

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GENENTECH, INC., a Delaware Corporation,
*Plaintiff*,

vs.

CELLTECH LIMITED, a British Company,
*Defendant*.

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# COMPLAINT FOR OVERTURNING A PATENT OFFICE DECISION IN AN INTERFERENCE

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Plaintiff, Genentech Inc. ("Genentech"), for its complaint against Defendant Celltech Limited ("Celltech"), alleges:

## *JURISDICTION*

1. This is an action for patent interference arising under the patent laws of the United States of America, particularly 35 U.S.C. § 146. This Court has jurisdiction of this action under 28 U.S.C. § 1338.

## *VENUE*

2. Venue lies in this District under 28 U.S.C. § 1391(b), (c) and (d).

## *PARTIES*

3. Plaintiff Genentech is a corporation duly organized and existing under the laws of Delaware and having its offices and principal place of business at One DNA Way, South San Francisco, California 94080.

4. Defendant Celltech is a British company having its offices and principal place of business at 216 Bath Road, Slough SL1 4EN, Berkshire, United Kingdom.

*CLAIM FOR RELIEF*

5. On April 8, 1983, Genentech, in the name of the inventors Shmuel Cabilly, Herbert L Heyneker, William E. Holmes, Arthur D. Riggs and Ronald B. Wetzel, filed an application for patent in the United States Patent and Trademark Office ("PTO"), which was given U.S. Serial No. 06/483,457. That application later issued as U.S. Patent 4,816,567, on March 28, 1989. Before issuance of that patent, a divisional application was filed on June 10, 1988, and was given Serial No. 07/205,419. These two applications are referred to as the "Cabilly" applications. The entire right, title, and interest in and to both of the Cabilly applications referred to in this paragraph were assigned, when filed, to Genentech.

6. Genentech, as the assignee of the entire right, title, and interest in and to the Cabilly applications identified in paragraph 5 above, has been and still is the owner of those applications. For those applications, Genentech was the owner of the entire right, title, and interest therein from the time they were filed, to the filing of this Complaint.

7. On November 14, 1984, Celltech, in the name of Michael A. Boss, John H. Kenten, John S. Emtage, and Clive R. Wood, as alleged co-inventors, filed an application in the PTO, and that application was given Serial No. 06/672.265. That application later issued as U.S. Patent 4,816,397 (the "Boss Patent"). on March 28. 1989. During proceedings in the PTO, Celltech was accorded the benefit of PCT application PCT/GB84/00094, filed March 23, 1984, and UK application No. 83/08235, filed March 25, 1983. These applications are referred to as the "Boss" applications. All three Boss applications were assigned to Celltech at the time

they were originally filed in 1983 and 1984, and since then the entire right, title and interest in the Boss applications and the Boss Patent has been owned by Celltech. Celltech was "the party in interest as shown by the records of the Patent and Trademark Office at the time of the decision complained of" herein (see 35 U.S.C. § 146).

8. As of August 13, 1998, the date of the decision complained of herein, the real parties in interest were Genentech and Celltech.

9. On or about March 9, 1990, Genentech, through an attorney, copied Claims 1-20 from the Boss Patent, for the purpose of provoking an interference. Claim 1 of the Boss Patent became the count of the interference. Pursuant to 35 U.S.C. § 135, an interference (No. 102,572) was declared on February 28, 1991, between the Cabilly application Serial No. 07/205,419, and the Boss Patent. The PTO found that an interference existed between claims 1-20 of the Boss Patent, on the one hand, and claims 101-120 of Cabilly application Serial No. 07/205,419, on the other hand.

10. Genentech's inventors, Shmuel Cabilly, Herbert L Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel, were the first inventors of the subject matter of the interference, and the inventors of the Boss Patent are not entitled to priority over the inventors in the Cabilly applications

11. The Boss inventors were not entitled to the award of priority for the reasons enumerated below, as well as such other and further reasons as will appear is the case proceeds.

12. Despite Boss never contesting that the Cabilly applications disclosed the invention of the count, and the earliest Cabilly application being filed less than two weeks after the earliest Boss application, the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office (the "Board") rendered a final decision on August 13.

1998 (copy attached and marked as Exhibit A) awarding priority of the count in issue to the senior party, Boss. Genentech is dissatisfied with the decision of the Board and therefore has filed this action under 35 U.S.C. § 146. This decision of the Board was erroneous in both law and fact:

a. The Board wrongfully found that Cabilly did not prove, by a preponderance of evidence, an actual reduction to practice of the invention in issue prior to March 25, 1983, the filing date of the earliest Boss application;

b. The Board wrongfully found that the Cabilly record failed to show possession of the essential elements of the count in interference, namely production of molecules recited in the process of the count, and that the product of the process was useful; and

c. The Board also wrongfully found that Cabilly failed to show a complete conception of the count prior to the March 25, 1983, date accorded Boss.

WHEREFORE, Genentech prays:

1. That this Court reverse the decision of the Board dated August 13, 1998.

2. That this Court declare that Shmuel Cabilly, Herbert L Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel are the original and first inventors of the subject matter of claims 101-120 of the Cabilly application and claims 1-20 of the Boss Patent, that Cabilly is entitled to a patent containing the Cabilly claims mentioned in this prayer, and that the claims of the Boss Patent are unpatentable to Boss.

3. That this Court authorize the Commissioner of Patents and Trademarks to grant Cabilly a patent on their application Serial No. 07/205,419, containing claims 101-120.

4. That this Court award costs of suit and such further relief as may be necessary and proper.

Dated: October 9, 1998 Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.
R. Danny Huntington
Mary Ann Dillahunty
LATHAM & WATKINS
Paul H. Dawes
Alexander S. Pesic

By: /s/ Paul H. Dawes
Paul H. Dawes
Attorneys for Plaintiff
GENERTECH, INC.

[*Exhibit 2 to Winters Declaration*]

Genentech Inc.

February 25, 1983

Dr. Arthur Riggs
City of Hope National Medical Center
1500 East Duarte Road
Duarte, CA 91001

Dear Dr. Riggs,

Enclosed for your review is the present draft of the patent application on the Recombinant Antibodies. Herb thought it appropriate to forward it to you at this point, although there is more material to be added to the Examples section.

Any suggestions or comments you or Schmuel may have would be welcome. I know there are data just arrived from Schmuel which are not included in this draft.

Sincerely

/s/ Kate H. Murashige
KATE H. MURASHIGE
Patent Attorney

## *Recombinant Hybrid Antibodies and Active Antibody Fragments* *

### *Background of the Invention*

This invention relates to the field of antibody production and to modification of naturally occuring antibody amino acid sequences. Specifically, the invention relates to useing recombinant techniques to produce both antibodies which are analogous to those normally found in mammalian systems and to take advantage of gene modification techniques to construct hybrid or other modified forms of antibodies.

### A. *Mammalian Antibodies*

Antibodies are polypeptides produced by the mammalian immune system in response to challenge by foreign proteins, glycoproteins, cells, or other antigenic foreign substances. The sequence of events which permits the organism to overcome invasion by foreign cells or to rid the system of foreign substances is at least partially understood. An important part of this process is the manufacture of antibodies which bind specifically to a particular foreign substance. The binding specificity of such polypeptides to a particular antigen is highly refined, and the multitude of specificities capable of being generated by the individual mammal is remarkable in its complexity and variability. Thousands of antigens are capable of eliciting responses, each almost exclusively directed to the particular antigen which elicited it.

#### A.1. *Source and Utility*

Two major sources of mammalian antibodies are presently known—generation in site by the mammalian B lymphocytes and in cell culture by hybridomas. Antibodies are made in situ as a result of the differentiation of B lymphocytes which occurs in response to stimulation by specific antigens. In the

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* Handwritten marks illegible and omitted.

undifferentiated B cell, the portions of DNA coding for the various sequences on the antibody chains are separated in the genomic DNA. In response to antigen stimulation, certain of the sequences are reassembled sequentially prior to transcription. A review of this process has been given by Gough _____(1981). The resulting genome is capable of expression in the mature B lymphocyte to produce the desired antibodies. Even when only a single antigen is introduced into the sphere of the immune system for a particular mammal, the antibodies generated in response differ somewhat in their range of capability for cross reacting with other, similar, antigens, since slightly differing arrangements of the genome of the mature B cell are responsible for each production sequence, i.e., the antibodies are "polyclonal".

This limited but inherent heterogeneity has been overcome in numerous particular cases by use of hybridoma technology to create "monoclonal" antibodies. In this process, the serum from a mammal which has been injected with antigen is fractionated to recover antibody-producing mature B cells, and this mixture of B cells fused with a tumor cell line, thus producing a hybrid or 'hybridoma" which is both immortal and capable of producing the genetically coded antibody of the B cell. The hybrids thus formed are segregated into single genetic strains by dilution and regrowth, and each strain thus represents a single genetic line. They therefore produce immunoactive antibodies against a desired antigen which are assured to be homogenous, and which antibodies, referencing their pure genetic parentage, are called "monoclonal". Hybridoma technology has to this time been largely focused of fusion murine lines, but human-human hybridomas, and human-murine hybridomas have been prepared as well.

Polyclonal, or, much more preferably, monoclonal, antibodies have a variety of useful properties similar to those of the present invention. For example, they can be used as specific immunoprecipitating reagents to detect the presence

of the antigen which elicited the initial formation of the B cell genome by coupling this reaction with suitable detection techniques such as labeling with radioisotopes or with enzymes capable of assay (RIA, EMIT, and ELISA). These antibodies are thus the foundation of diagnostic tests for these antigenic substances. In another important use, such antibodies can be directly injected into subjects suffering from an attack by a substance or organism containing the antigen in question to combat this attack. This process is currently in its experimental stages, but its potential is clearly seen. Third, whole body diagnosis and treatment is made possible because injected antibodies are directed to specific target disease tissues which have proper antigenic surfaces, and can be used either to determine the presence of the disease by carrying with them a suitable label, or to attack the diseased tissue by carrying a suitable drug.

Monoclonal antibodies produced by hybridomas, while theoretically effective as suggested above and clearly preferable to polyclonals because of their specificity, suffer from certain disadvantages. First, they tend to be contaminated with other proteins and cellular materials of hybridoma, (and, therefore, mammalian) origin. This is particularly serious because of the nature of the cells used to immortalize the hybridoma cell lines, which are, of course, themselves malignant. These cells contain additional materials, notably nucleic acid fragments, but protein fragments as well, which are capable of enhancing, causing, or mediating carcinogic responses. Second, hybridoma lines producing monoclonals tend to become unstable after several generations of production and to alter the structure of antibody produced. The cell line genome appears to alter itself in response to stimuli whose nature is not currently known, and this alteration results production of incorrect sequences. Third, both hybridoma and B cells inevitably produce certain antibodies in glycosylated form which, under some circumstances, is undesirable. Fourth, production of both monoclonals and poly-

clonals is relatively expensive. Fifth, and perhaps most important, production by current techniques (either by hybridoma or by B cell response) does not permit manipulation of the genome so as to produce antibodies with more effective design components than those normally elicited in response to antigens from the mature B cell in situ. The antibodies of the present invention do not suffer from the foregoing drawbacks, and, furthermore, offer the opportunity to provide molecules of superior design.

A.2 *General Structure Characteristics*

The general structure of antibody molecules in mammalian systems is now well understood. They are composed of two identical light polypeptide chains of molecular weight approximately 23,000 daltons, and two identical heavy chains of molecular weight 53,000-70,000. The four chains are joined by disulfide bonds in a "Y" configuration wherein the light chains bracket the heavy chains starting at the mouth of the Y and continuing through the divergent region as shown in figure 1. The "branch" portion, as there indicated, is designated the Fab region. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, with some subclasses among them, and the nature of this chain, as it has a long constant region, determines the "class" of the antibody as IgG, IgM, IgA, IgD, or IgE. Light chains are classified as either kappa or lambda. Each heavy chain class can be prepared with either kappa or lambda light chain. The light and heavy chains are covalently bonded to each other, and the "tail" portions of the two heavy chains are bonded to each other by covalent disulfide linkages when the antibodies are generated either by hybridomas or by B cells. However, if non-covalent association of the chains can be effected in the correct geometry, the aggregate will still be capable of reaction with antigen.

The amino acid sequence runs from the N-terminal end at the top of the Y to the C-terminal end at the bottom of each

chain. At the N-terminal end is a variable region which is specific for the antigen which elicited it, and is approximately 100 amico acids in length, there being slight variations between light and heavy chain and from antibody to antibody. The variable region is linked in each chain to a constant region which extends the remaining length of the chain through a linking sequence known currently as the "C" region in the light chain, comprising about 12 amino acids, and as a combination of "D" region and "J" region in the heavy chain, comprising around 25 amino acids.

The remaining portions of the chain are referred to as constant regions and within a particular class appear not to vary, at least very much, with the specificity of the antibody (i.e., the antigen eliciting it).

At present there are five known major classes of constant regions which determine the class of the immunoglobulin molecule (IgG, IgM, IgA, IgD, and IgE corresponding to $\gamma$, $\mu$, $\alpha$, $\delta$, and $\varepsilon$ heavy chain constant regions). The constant region or class seems to determine the effector function of the antibody i.e., activation of complement, release of histamine, etc. As mentioned above, the variable region determines the antigen with which it will react.

B. *Recombinant DNA Technology*

Recombinant DNA technology has reached sufficient sophistication that it includes a repertoire of techniques for cloning and expression of gene sequences. Various DNA sequences can be recombined with some facility, creating new DNA entities capable of producing heterologous protein product in transformed microbes and cell cultures. The general means and methods for the *in vitro* ligation of various blunt ended or "sticky" ended fragments of DNA, of producing expression vectors, and of transforming particular organisms, to direct synthesis of desired product are in hand. However, on an individual product basis, the pathway remains tortuous and unchartable in advance and the science

has not advanced to a stage where predictions of success can to made. Indeed, those who portend successful results without the underlying experimental basis, do so at considerable risk of inoperability.

DNA recombination of the essential elements, i.e., an origin of replication, one or more phenotypic selection characteristics, expression control sequence, heterologous gene insert and remainder vector, generally is performed outside the host cell. The resulting recombinant replicable expression vector, or plasmid, is introduced into cells by transformation and large quantities of the recombinant vehicle is obtained by growing the transformant. Where the gene is properly inserted with reference to portions which govern the transcription and translation of the encoded DNA message, the resulting expression vector is useful to produce the polypeptide sequence for which the inserted gene codes, a process referred to as "expression." The resulting product may be obtained by lysis, if necessary, of the host cell and recovery of the product by appropriate purifications from other proteins.

In practice, the use of recombinant DNA technology can express entirely heterologous polypeptides—so-called direct expression—or alternatively may express a heterologous polypeptide fused to a portion of the amino acid sequence of a homologous polypeptide. In the latter cases, the intended bioactive product is sometimes rendered bioinactive within the fused, homologous/heterologous polypeptide until it is cleaved in an extracellular environment.

The art of maintaining cell or tissue cultures as well as microbial systems for studying genetics and cell physiology is well established. Means and methods are available for maintaining permanent cell lines, prepared by successive serial transfers from isolated cells. For use in research, such cell lines are maintained on a solid support in liquid medium,

or by growth in suspension containing support nutriments. Scale-up for large preparations seems to pose only mechanical problems.

*Summary of the Invention*

The invention relates to antibodies formed by recombinant techniques using suitable host cell cultures. These antibodies can be prepared in pure form, and, further, can be manipulated at the genomic level to produce hybrids of variants which draw their homology from species which differ from each other. Thus, there are a number of "types" of antibodies encompassed by the invention. First, antibodies are produced using recombinant techniques which mimic the amino acid sequence of naturally occuring antibodies produced by either mammalian B cells *in situ*, or by B cells fused with suitable tumor immortalizing lines, i.e., hybridomas. Second, the methods of this invention produce, and the invention is directed to, antibodies which comprise light chains whose amino acid sequence mimics that of one naturally occuring antibody, and heavy chains whose amino acid sequence mimics the heavy chain of another. The antibody chains so mimicked may be of different species, i.e. "composite antibodies" especially "divalent" antibodies. Third, by genetic manipulation, "hybrid" antibodies can be formed wherein variable regions correspond to the amino acid sequence from one mammalian model system, whereas the constant region mimics the amino acid sequence of another. Again, the derivation of these two mimicked sequences may be from different species. Fourth, antibodies may be produced which include only the "Fab" region of an antibody molecule i.e. the branches of the antibody "Y". These Fab fragments may also be composite—i.e., one chain derived from one model antibody and the other from another, each of different species, or hybrid, where the constant and variable sequence patterns may be of different origin. Finally, either the light chain or heavy chain alone, or active portions thereof,

produced by recombinant techniques are included in the invention.

In other aspects, the invention is directed to DNA which encodes the aforementioned antibodies and portions thereof, as well as expression vectors or plasmids capable of effecting the production of such antibodies in suitable host cells. It includes the host cells and cell cultures which result from transformation with these vectors. Finally, the invention is directed to methods of producing these antibodies, and the DNA sequences, plasmids, and transformed cells intermediate to them.

*Brief Description of the Drawings*

Figure 1 is a representation of the general structure of mammalian antibodies.

Figure 2 shows the detailed sequence of the cDNA insert of pK17G04 which encodes kappa anti CEA chain.

Figure 3 shows the coding sequence of the fragment shown in Figure 2, along with the corresponding amino acid sequence.

Figure 4 shows this DNA fragment encoding gamma anti CEA chain.

Figure 5 shows the corresponding amino acid sequence encoded by the fragment in Figure 4.

Figures 6 and 7 outline the construction of expression vectors for kappa and gamma anti CEA respectively.

*Detailed Description*

A. Definitions

As used herein, "antibodies" refers to tetramers which have specific immunoprecipitating activity comprising two light chains of approximately 25kD and two heavy chains of approximately 50-70kD, aggregated in the "Y" configuration of figure 1, with or without covalent linkage between them.

"Mammalian antibodies" refers to antibodies wherein the amino acid sequences of the chains are homologous with those sequences found in antibodies produced by mammalian systems, either in situ, or in hybridomas. These antibodies mimic antibodies which are otherwise capable of being generated, although in impure form, in these traditional systems.

"Composite antibodies" refer to antibodies wherein chains are separately homologous with referenced mammalian antibody chains. For example, while the light chains are homologous to sequences found in one type of mammalian derived antibodies, the heavy chains might mimic another. However, in a preferred embodiment of composite antibody, "divalent" antibodies result. In this embodiment, one pair of heavy chain is homologous to antibodies raised against one antigen, while the other pair of heavy and light chain is homologous to those raised against another antigen. This results in the property of "divalence" i.e., ability to bind two antigens simultaneously.

"Hybrid antibodies" refers to those antibodies wherein one portion of each of the amino acid sequences of heavy and light chains is homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular class, while the remaining segment of the chains is homologous to corresponding sequences in another. Typically, in these hybrid antibodies, the variable region of both light and heavy chains mimics the variable regions of antibodies derived from one species of mammals, while the constant portions are homologous to the sequences in antibodies derived from another. However, the definition is not limited to this particular example. It includes any antibody in which either or both of the heavy or light chains are made up from combinations of sequences mimicking the sequences in antibodies of different sources, whether these sources be differing classes, differing antigen responses, or differing species of origin.

"Fab region" refers to those portions of the chains which are roughly equivalent or analogous to the sequences which comprise the Y branch portions of the heavy chain and the light chain in its entirety. "Fab region" includes aggregates of one heavy and the light chain, as well as tetramers which correspond to the two branch segments of the antibody Y, whether any of the above are covalently or non-covalently aggregated, so long as the aggregation is capable of selectively reacting with a particular antigen or antigen family.

"Fab region" has the same subsets according to the definition of the present invention as does the general term "antibodies". Thus, "mammalian Fab region", "composite Fab region", and "hybrid Fab region" are defined analogously to the corresponding definitions set forth in the previous paragraphs for the various types of antibodies.

Individual heavy or light chains may of course be either "mammalian" or "hybrid" in accordance with the above. As will become apparent from the detailed description of the invention, it is possible, using the techniques disclosed to prepare other combinations of the four-peptide chain aggregates, besides those specifically defined such as composite antibodies containing hybrid light and mammalian heavy chains, composite Fab regions containing hybrid Fab regions of heavy chains associated with mammalian light chains, and so forth.

"Expression vector" includes vectors which are capable of expressing DNA sequences contained therein, i.e., the coding sequences are operably linked to other sequences capable of effecting their expression. It is implied, although not always explicitly stated, that these expression vectors must be replicable in the host organisms either as episomes or as an integral part of the chromosomal DNA. Clearly a lack of replicability would render them effectively inoperable. A useful, but not a necessary, element of an effective expression vector is a marker encoding sequence—i.e. sequences en-

coding a protein which results in a phenotypic property (e.g. tetracycline resistance) of the cells containing them which permits those cells to be readily identified. In sum, "expression vector" is given a functional definition, and any DNA sequence which is capable of effecting expression of a specified contained DNA code is included in this term, as it is applied to the specified sequence. As at present, such vectors are frequently in the form of plasmids, plasmic and expression vector are often used interchangeably. However, the invention is intended to include such other forms of expression vectors which serve equivalent functions and which may, from time to time become known in the art.

"Recombinant host cells" refers to cells which have been transformed with vectors constructed using recombinant DNA techniques. As defined herein, the antibody or modification thereof produced by a recombinant host cell is by virtue of this transformation, rather than in such lesser amounts, or more commonly, in such less than detectable amounts, as would be produced by the untransformed host.

In descriptions of processes for isolation of antibodies from recombinant hosts, the terms "cell" and "cell culture" are used interchangeably to denote the source of antibody unless it is clearly specified otherwise. In other words, recovery of antibody from the "cells" may mean either from spun down whole cells, or from the cell culture containing both the medium and the suspended cells.

3. *Host Cell Cultures and Vectors*

The vectors and methods disclosed herein are suitable for use in host cells over a wide range of prokaryotic and eukaryotic organisms.

In general, of course, prokaryotes are preferred for cloning of DNA sequences in constructing the vectors useful in the invention. For example, *E. coli* K12 strain 294 (ATCC No. 31446) is particularly useful. Other microbial strains which

may be used include *E. coli* strains such as *E. coli* 8, and *E. coli* 1776 (ATTC No. 31537). These examples are, of course, intended to be illustrative rather than limiting.

Prokaryotes may also be used for expression. The aforementioned strains, as well as *E. coli* W3110 (Fλ, prototrophic, ATTC No. 27325), bacilli such as *Bacillus subtilus*, and other entercoacteriaceae such as *Salmonella typhimurium* or *Serratia marcesans*, and various *Pseudomonas* species may be used.

In general, plasmid vectors containing replicon and control sequences which are derived from species compatible with the host cell are used in connection with these hosts. The vector ordinarily carries a replication site, as well as marking sequences which are capable of providing phenotypic selection in transformed cells. For example, *E. coli* is typically transformed using p8R322, a plasmic derived from an *E. coli* species (Bolivar, et al., *Gene* 2: 95 (1977)). pBR322 contains genes for ampicillin and tetracycline resistance and thus provides easy means for identifying transformed cells. The pBR322 plasmid, or other microbial plasmid must also contain, or be modified to contain, promoters which can be used by the microbial organism for expression of its own proteins. Those promoters most commonly used in recombinant DNA construction include the β-lactamase (penicillinase) and lactose promoter systems (Chang et al, *Nature*, 275: 615 (1978); Itakura, et al, *Science*, 198: 1056 (1977); (Sceddel, et al *Nature* 981: 544 (1979)) and a tryptophan (trp) promoter system (Goeddel, et al, *Nucleic Acids Res.*, 8: 4057 (1980); EPO Appl Publ No. 0036776). While these are the most commonly used, other microbial promoters have been discovered and utilized, and details concerning their nucleotide sequences have been published, enabling a skilled worker to ligate them functionally with plasmid vectors Siebenlist, et al. *Cell* 26: 269 1980.

In addition to prokaryates, eukaryotic microbes, such as yeast cultures may also be used. *Saccharomyces cerevistae*, or common baker's yeast is the most commonly used among eukaryotic microorganisms, although a number of other strains are commonly available. For expression in *Saccharomyces*, the plasmid YRp7, for example, (Stinchcomo, et al, *Nature*, 282: 39 (1979); Kingsman et al, *Gene*, 7: 141 (1979); Tschemper, et al, *Gene*, 10: 157 (1980)) is commonly used. This plasmid already contains the *trpl* gene which provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example ATCC No. 44076 or PEP4-1: (Jones, *Genetics*, 85: 12 (1977)). The presence of the *trpl* lesion as a characteristic of the yeast host cell genome then provides an effective environment for detecting transformation by growth in the absence of tryptophan.

Suitable promoting sequences in yeast vectors include the promoters for 3-phosphoglycerate kinase (Hitzeman, et al., *J. Biol. Chem.*, 255: 2073 (1980)) or other glycolytic enzymes (Hess, et al, *J. adv. Enzyme Reg.*, 7: 149 (1968); Holland, et al, Biochemistry, 17: 4900 (1978)), such as enolase glyceraldehydes-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-δ-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglusoce isomerase, and glucokinase. In constructing suitable expression plasmids, the termination sequences associated with these genes are also ligated into the expression vector 3 of the sequence desired to be expressed to provide polyadenylation of the mRNA and termination. Other promoters, which have the additional advantage of transcription controlled by growth conditions are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase degradative enzymes associated with nitrogen metapolism, and the aforementioned glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization (Holland, ioid.). Any plasmid vector containing yeast-

compatible promoter, origin of replication and termination sequences is suitable.

In addition to microorganisms, cultures of cells derived from multicellular organisms may also be used as hosts. In principle, any such cell culture is workable, whether from vertebrate or invertebrate culture. However interest has been greatest in vertebrate cells, and propogation of vertebrate cells in culture (tissue culture) has become a routine procedure in recent years (*Tissue Culture*, Academic Press, Kruse end Patterson, editors (1973)]. Examples of such useful host cell lines are VERO and HeLa cells, Chinese hamster ovary (CHO) cell lines, and W138, BHK, COS-7 and MDCK cell lines. Expression vectors for such cells ordinarily include (if necessary) an origin of replication, a promoter located in front of the gene to be expressed, along with any necessary ribosome binding sites, RNA splice sites, polyadenylation site, and transcriptional terminator sequences.

For use in mammalian cells, the control functions on the expression vectors are often provided by viral material. For example, commonly used promoters are derived from polyoma, Adenovirus 2, and most frequently Simian Virus 40 (SV40). The early and late promoters of SV40 virus are particularly useful because both are obtained easily from the virus as a fragment which also contains the SV40 viral origin of replication (Fiers, et al. *Nature*, 273: 113 (1978)) incorporated herein by reference. Smaller or larger SV40 fragments may also be used, provided there is include [*sic*] the approximately 250 bp sequence extending from the Hind III site toward the Bgl I site located in the viral origin of replication [*sic*]. Further, it is also possible, and often desirable, to utilize promoter or control sequences normally associated with the desired gene sequence, provided such control sequences are compatible with the host cell systems.

An origin of replication may be provided either by construction of the vector to include an exogenous origin,

such as may be derived from SV40 or other viral (e.g. Polyoma, Adeno, VSV, BPV, etc.) source, or may be provided by the host cell chromosomal replication mechanism. If the vector is integrated into the host cell chromosome, the latter is often sufficient.

It will be understood that this invention, although described herein in terns of a preferred embodiment, should not be construed as limited to those host cells, vectors and expression systems exemplified.

C. *Methods Employed*

C.1 *Transformation*:

If cells without formidable cell wall barriers are used as host cells, transfection is carried out by the calcium phosphate precipitation method as described by Graham and Van der Eb, *Virology*, 52: 546 (1978). However, other methods for introducing DNA into cells such as by nuclear injection or by protoplast fusion may also be used.

If prokaryotic cells or cells which contain substantial cell wall constructions are used, the preferred method of transfection is calcium treatment using calcium chloride as described by Cohen, F.N. et al *Proc. Natl. Acad. Sci.* (USA), 69: 2110 (1972).

C.2 *Vector Construction*

Construction of suitable vectors containing the desired coding and control sequences employ standard ligation techniques. Isolated plasmids or DNA fragments are cleaved, tailored, and religated in the form desired to form the plasmids required. The methods employed are not dependent on the DNA source, or intended host.

Cleavage is performed by treating with restriction enzyme, (or enzymes) in suitable buffer. In general, about 1 μg plasmid or DNA fragments is used with about 1 unit of enzyme in about 20 μl of buffer solution. (Appropriate buffers and

substrate amounts for particular restriction enzymes are specified by the manufacturer. Incubation times of about 1 hour at 37°C are workable. After incubations, protein is removed by extraction with phenol and chloroform, and the nucleic acid is recovered from the aqueous fraction by precipitation with ethanol.

If blunt ends are required, the preparation is treated for 15 minutes at 15° with 10 units of *E. coli* DNA Polymerase 1 (Klenow), phenol-chloroform extracted, and ethanol precipitated.

Size separation of the cleaved fragments is performed using 6 percent polyacrylamide gel described by Goeddel, D., et al, *Nucleic Acids Res.* 8: 4057 (1980) incorporated herein by reference.

For ligation, approximately equimolar amounts of the desired components, suitably end tailored to provide correct matching are treated with about 10 units T4 DNA ligase per 0.5 μg DNA. (When cleaved vectors are used as components, it may be useful to prevent religation of the cleaved vector by pretreatment with bacterial alkaline phosphatase.)

In the examples described below correct ligations for plasmid construction are confirmed by transforming *E. coli* K12 strain 294 (ATCC 31446) with the ligation mixture. Successful transformants were selected by ampicillin or tetracycline resistance depending on the mode of plasmid construction. Plasmids from the transformants were then prepared, analyzed by restriction and/or sequenced by the method of Messing, et al, *Nucleic Acids Res.*, 9:309 (1981) or by the method of Maxam, et al, *Methods in Enzymology*, 65: 499 (1980).

D. *Outline of Procedures*

D.1 *Mammalian Antibodies*

The first type of antibody which forms a part of this invention, and is prepared by the methods thereof, is "mammalian antibody" one wherein the heavy and light chains mimic the amino acid sequences of an antibody otherwise produced by a mature mammalian 8 lymphocyte either *in situ* or when fused with an immortalized cell as part of a hydridoma culture. In outline, these antibodies are produced as follows:

Messenger RNA coding for heavy or light chain is isolated from a suitable source, either mature B cells or a hydridoma culture, employing standard techniques or RNA isolation, and the use of oligo—dT cellulose chromatography to segregate the poly-A mRNA. The poly-A mRNA may, further, be fractionated to obtain sequences of sufficient size to code for the amino acid sequences in the light or heavy chain of the desired antibody as the case may be.

A cDNA library is then prepared from the mixture of mRNA using a suitable primer, preferably a nucleic acid sequence which is characteristic of the desired cDNA. Such a primer may be hypothesized and synthesized based on the amino acid sequence of the antibody if the sequence is known. In the alternative cDNA from unfractionated poly-A mRNA from a cell line producing the desired antibody or poly-dT may also be used. The resulting cDNA is optionally size fractionated on polyacrylamide gel and then extended with, for example, dC residues for annealing with pBR322 or other suitable cloning vector which has been cleaved by a suitable restriction enzyme, such as Pst I, and extended with dG residues. Alternative means of forming cloning vectors containing the cDNA using other tails and other cloning vector remainder may, of course, also be used but the foregoing is a standard and preferable choice. A suitable host

cell strain, typically *E. coli*, is transformed with the annealed cloning vectors, and the successful transformants identified by means of, for example, tetracycline resistance or other phenotypic characteristic residing on the cloning vector plasmid.

Successful transformants are picked and transferred to microtiter dishes or other support for further growth and preservation. Nitrocellulose filter imprints of these growing cultures are then probed with suitable nucleotide sequences containing bases known to be complementary to desired sequences in the cDNA. Several types of probe may be used, preferably synthetic single stranded DNA sequences labeled by kinasing with $ATP^{32}$. The cells fixes to the nitrocellulose filter are lysed, the DNA denatured, and then fixed before reaction with kinased probe. Clones which successfully hybridize are detected by contact with a photoplate, then plasmids from the growing colonies isolated and sequenced by means known in the art to verify that the desired portions of the gene are present.

The desired gene fragments are excised and tailored to assure appropriate reading frame with the control segments when inserted into suitable expression vectors. Typically, nucleotides are added to the 5' end to include a start signal and a suitably positioned restriction endonuclease site.

The tailored gene sequence is then positioned in a vector which contains a promoter in reading frame with the gene and compatible with the proposed host cell. A number of plasmids such as those described in U.S. Pat. Application Ser. No. 307473; 291892; and 305657, have been described which already contain the appropriate promoters, control sequences, ribosome binding sites, and transcription termination sites, as well as convenient markers.

In the present invention, the gene coding for the light chain and that coding for the heavy chain are recovered separately by the procedures outlined above. Thus they may be inserted

into separate expression plasmids, or in tandem in the same plasmid, so long as each is under suitable promoter and translation control.

The expression vectors constructed above are then used to transform suitable cells. The light and heavy chains may be transformed into separate cell cultures, either of the same or of differing species; separate plasmids for light and heavy chain may be used to co-transform a single cell culture, or, finally, a single expression plasmid containing both genes and capable of expressing the genes for both light and heavy chain may be transformed into a single cell culture.

Regardless of which of the three forgoing options is chosen, the cells are grown under conditions appropriate to the production of the desired protein. Such conditions are primarily mandated by the type of promoter and control systems used in the expression vector, rather than by the nature of the desired protein. The protein thus produced is then recovered from the cell culture by methods known in the art, but choice of which is necessarily dependent on the form in which the protein is expressed. For example, it is common for mature heterologous proteins expressed in *E. coli* to be deposited within the cells as insoluble particles which require cell lysis and solubilization in denaturant to permit recovery. On the other hand, proteins under proper synthesis circumstances, in yeast and bacterial strains, can be secreted into the medium, or recovered by less drastic procedures. Tissue culture cells as hosts also appear, in general, to permit reasonably facile recovery of heterologous proteins.

When heavy and light chain are coexpressed in the same host, the isolation procedure is designed so as to recover reconstituted antibody. This is done by providing mild denaturing/renaturing conditions so as to permit such assembly. Typically, extraction in about 5 - 9M area in the presence of reducing agent, followed by dialysis into dilute buffer in the presence of air provides these conditions.

If the heavy and light chains are prepared in separate cell cultures, additional steps are required to secure the reconstitution of the two chains. This recombination can be effected as follows:

D.2 *Composite Antibodies*

The foregoing procedure which describes the recombinant production of mammalian antibodies is employed with some modifications to construct the remaining types of antibodies encompassed by the present invention. To prepare the embodiment of composite antibodies wherein the homology of the chains corresponds to the sequences of antibodies of different origins it is of course, only necessary to prepare the heavy and light chains in separate cultures and reassemble them as desired.

For example, in order to make a murine light chain-human heavy chain composite antibody, a suitable murine source for the mRNA used as a template for the light chain clone would comprise one of the many available murine-murine hybridomas, or even a murine-human hybridoma wherein the B cell is murine derived and the myeloma from human beings. The heavy chain would need to be derived from a human-human hybridoma, or at least one in which the B cell was of human origin in order to provide the mRNA for the heavy chain. It is clear that such composites can be assembled using the methods of the invention almost at will, and are limited only by available sources of mRNA suitable for use as templates for the respective chains. All other features of the process are similar to those described above.

Divalent antibodies are particularly useful as they are capable of simultaneous reaction with more than one antigen. Again, heavy and light chaines [*sic*] corresponding, in the prefered embodiment to the chains of antibodies of the same origin are prepared in separate cultures. Two such sets are prepared. The separate preparation of heavy and light chains

prevents premature assembly of the tetramer. Subsequent mixing of the four separately prepared peptides then permits assembly into the desired tetramers. While random aggregation will lead to the formation of some byproduct mammalian antibodies, approximately half of the product in which homologously desired light and heavy chains are bound to each other is the desired divalent antibody.

D.3 *Hybrid Antibodies*

For construction of hybrid antibodies (wherein, for example, the variable sequences are separately derived from the constant sequences) the procedures of paragraph D.1 are again applicable with appropriate additions and modifications. A preferred procedure is to recover desired portions of the genes encoding for parts of the heavy and light chains from suitable, differing sources and then to religate these fragments using restriction endonucleases to reconstruct the gene coding for each chain.

For example, in a particularly uncomplex preferred hybrid construction, portions of the heavy chain gene and of the light chain gene which encode the variable sequences of antibodies produced by a murine hybridoma culture are recovered and cloned from the murine culture and gene fragments encoding the contant [*sic*] regions of the heavy and light chains for human antibodies are recovered and cloned from for example, a human-human hybridoma. Suitable restriction enzymes may then be used to ligate the variable portions of the mouse gene to the constant regions of the human gene for each of the two chains. The hybrid chains are produced as set forth in D.1, aggregated and used in the same manner as the non-hybrid forms.

D.4 *Fab Region*

Similarly, it is not necessary to include the entire gene for the heavy chain portion. All of the aforementioned variations can be superimposed on a procedure for Fab region pro-

duction and the overall procedure differs only in that that portion of the heavy chain coding only for the first approximately 220 amino acids of the heavy chain is employed in the expression vector.

E. *Specific Examples of Preferred Embodiments*

The invention has been described above in general terms and there follow several specific examples of embodiments of this invention which set forth details of experimental procedure in producing the desired antibodies. Example E.1 sets forth the general procedure for preparing anti CEA antibody, a "mammalian antibody". Example E.3 sets forth the procedure for tailoring the heavy or light chain so that the variable and constant regions may be derived from different sources. When combined with the procedure in example E.1, this exemplifies the production of the hybrid antibodies. Example E.4 sets forth the method of obtaining a shortened heavy chain genome which permits the production of the Fab regions. Composite antibodies and Fab regions differ only in the choice source materials for heavy and light chains, as set forth in E.4.

The examples set forth below are for illustrative purposes and do not limit the scope of the invention.

E.1 *Preparation of Expression Vectors for Murine anti-CEA Antibody Chains and Peptide Synthesis*

Carcinoembryonic antigen (CEA) is associated with the surface of tumor cells in post-natal mammals. Antibodies which bind to it (anti-CEA) antibodies) [*sic*] are useful in detection and treatment of certain mammalian tumors which appear to support CEA at their surfaces. A mouse hybridoma cell line $SP_2$-014 Ag which secretes anti-CEA antibodies has been prepared as described by ___.

E.1.1 *Isolation of Messenger RNA for Anti CEA-Kappa and Gamma Chains*

Total RNA from $SP_2$-014Ag cells was extracted essentially as reported by Lynch et al, ___. Cells were pelleted by centrifugation and approximately 1 g portions of pellet resuspended in 10 ml of 10 mM NaCl, 10 mM Tris HCl (pH 7.4), 1.5 mM $MgC1_2$. The resuspended cells were lysed by addition of non-ionic detergent NP-40 to a final concentration of 1 percent, nuclei removed by centrifugation and the supernatant extracted twice with ___ml portions of phenol (redistilled)/chlroform: isoamyl alcohol ___:___ at 4°C. The aqueous phase was made O.2 M in NaCl and total RNA was precipitated by addition of two volumes of 100 percent ethanol and overnight storage at -20°C. After centrifugation, polyA mRNA was purified from total RNA by oligo-dT cellulose chromatography as described by ___. 10-15 mg of total RNA containing -2 percent polyA mRNA was obtained from 1g cells.

E.1.2 *Preparation of Oligo-dT Primed Colony Library Containing Kappa and Gamma DNA Sequences*

5 μg of the unfractionated polyA mRNA prepared in paragraph E.1.1 was used as template for oligo-dT primed preparation of double-stranded (ds) cDNA by standard procedures as described by Goeddel et al., *Nature* 281: 544 (1979) and Wickens et al., *J. Biol. Chem.* 253: 2483 (1978) incorporated herein by reference. The cDNA was size fractionated by a percent polyacrylamide gel electrophoresis and 124 ng of ds cDNA greater than 600 base pairs in length was recovered by electruelution. A 20 ng portion of ds dDNA was extended with deoxy C residues using terminal deoxynucleotidyl transferase as described in Chang et al., *Nature* 275: 617 (1978) incorporated herein by reference, and annealed with 200 ng of the plasmid pBR322 (Bolivar et al., *Gene* 2: 95 (1977)): which had been cleaved with Pst I and tailed with deoxy G. Each annealed mixture was then transformed into *E. coli* K12

strain 294 (ATCC No. 31446). Approximately 7500 ampicillin sensitive, tetracycline resistant transformants were obtained.

E.1.3 *Preparation of Synthetic DNA Kappa and Gamma DNA Screening Probes*

The 14mer, 3' AGGTAGAAGGGTGG 5' complementary to the coding sequence of constant region for mouse MOPC21 kappa chain which begins 25 basepairs 3' of the variable region DNA sequence was used as kappa probe. A 15 mer, 3' GACCCTACGGACCAG 5', complementary to a coding sequence located 72 basepairs 3' of the variable region DNA sequence for mouse MOPC21 gamma chain was used to probe gamma.

Both probes were synthesized by the phospnotriester method described in German Offenlegungschrift 2644432, incorporated herein by reference, and made radioactive by kinasing as follows: 250 ng of deoxyoligonucleotide were combined in 25 µl of 60 mM Tris HCl (pH 8), 10 mM $MgCl_2$, 15 mM beta-mercaptoethanol, and 100 µCi ($\gamma$-$^{32}$P) ATP (Amersham, 5000 Ci/mMole). 5 units of T4 polynucleotide kinase were added and the reaction was allowed to proceed at 37°C for 30 minutes and terminated by addition of EDTA to 20mM.

E.1.4 *Screening of Oligo dT Primed Colony Library for Kappa or Gamma Sequences*

-2000 colonies of the transformants prepared as described in paragraph E.1.2 were individually inoculated into wells of microtitre dishes containing L8 (Miller, Experiments in Molecular Genetics, p. 431-3, Cold Spring Harbor Lab., Cold Spring Harbor, New York (1972)) 5µg/ml tetricycline and stored at -20°C after addition of DMSO to 7 percent. Individual colonies from this library were transferred to duplicate sets of Scleicher and Schuell 8A85/20 nitrocellulose filters and grown on agar plates containing L8+5 µg/ml tetracycline. After -10 hours growth at 37°C the colony filters were

transferred to agar plates containing L8+5 μg/ml tetracycline and 12.5 μg/ml chloramphenical and reincubated overnight at 37°C. The DNA from each colony was then denatured and fixed to the filter by a modification of the Grunstein-Hogness procedure as described in Grunstein et al., *Proc. Nat'l Acad. U.S.A.* 72; 3961 (1975), incorporated herein by reference. Each filter was floated for 3 minutes on 0.6N NaOH,1.5 M NaCl to lyse the colonies and denature the DNA then neutralized by floating for 15' on 3 M NaCl, 0.5 M Tris HCl (pH 7.5). The filters were then floated for an additional 15 minutes on 2XSSC, and subsequently baked for 2 hours in an 80°C vacuum oven. The filters were prehybridized for -2 hours at room temperature in 0.9 M NaCl 1x Denhardts, 100 mM Tris HCl (pH 7.5), 5 mM Na-EDTA, 1 mM ATP, 1 M sodium phosphate (dibasic), 1 mM sodium pyrophosphate, 0.5 percent NP-40, and 200 μg/ml *E. Coli* t-RNA and hybridized in the same solution overnight, essentially as described by Wallace *et al. Nucleic Acids Research* 9: 879 (1981) using -40x$10^6$ cpm of either the kinased kappa or gamma probe described above.

After extensive washing at 37°C in 6X SSC, 0.1 percent SDS, the filters were exposed to Kodak XR-5 X-ray film with DuPont Lightning-Plus intensifying screens for 16-24 hours at -80°C. Approximately 20 colonies which hybridized with kappa probe and 20 which hybridized with gamma probe were found.

E.1.5 *Characterization of Colonies Indicating Positive Hybridization for Kappa DNA Sequence*

Plasmid DNAs isolated from several different transformed colonies which hybridized to kappa probe by the rapid miniscreen procedure of Birnboim et al., *Nucleic Acids Research*, 7: 1513 (1979), incorporated herein by reference, were cleaved with PSt I and fractionated on polyacrylamide gel. This analysis demonstrated that a number of plasmid DNAs contained cDNA inserts large enough to encode full

length kappa chain. The complete nucleotide sequence one of these plasmids (pK17G4) cDNA insert was determined by the dideoxynucleotide chain termination method as described by Smith, *Methods Enzymol. 65*, 560 (1980) incorporated herein by reference after subcloning restriction endonuclease cleavage fragments into M13 vectors (Messing et al., *Nucleus Acids Research* 9: 309 (1981), Figure 2 shows the nucleotide sequence of the cDNA insert of pK17G4 and Figure 3 shows the gene sequence with the corresponding amino acid sequence. Thus, the entire coding region of mouse anti-CEA kappa chain was isolated on this one large DNA fragment. The nucleotide sequence of the kappa probe includes nucleotides 377 through 390 of the pK17G4 insert which corresponds perfectly with the first 23 N-terminal amino acids of mature mouse anti-CEA kappa chain (as determined by amino acid sequence analysis of purified mouse anti-CEA kappa chain). The coding region of pK17G4 consists of 27 basepairs or 9 amino acids of the presequence and 648 basepairs or 226 amino acids of the mature protein. The mature protein has a variable region of 107 amino acids, a J1 joining region of 12 amino acids on a constant region of 107 amino acids. The stop codon after the C terminal amino acid 215 begins the 212 basepairs of 3' untranslated sequence up to the polyA addition.

E.1.6 *Characterization of Colonies Indicating Positive Hybridization for Gamma 1 DNA Sequence*

Plasmid DNA isolated from several transformants positive for hybridization with the gamma 1 prove was subjected to PSt I restriction endonuclease analysis as described in E.1.5. Plasmid DNAs demonstrating the largest cDNA insert fragments were selected for further study. Nucleotide sequence information for mouse gamma 1, shows an NcoI restrictiction endonuclease cleavage site near the junction between variable and constant region. Selected plasmid DNAs were digested with both PstI and NcoI and sized on polyacrylamide. This

analysis allowed identification of a number of plasmid DNAs that contain NcoI restriction endonuclease sites, although none that demonstrate cDNA insert fragments large enough to encode the entire coding region of mouse anti-CEA gamma 1 chain. Figure 4 presents the entire nucleotide sequence of mouse anti-CEA gamma 1 chain (as determined by dide oxynucleotide chain termination method of Smith, *Methods Enzymol*, 65:, 560 (1980)), and Figure 5 includes the translated sequence. In one plasmid isolated, p γ298 cDNA insert of about 1300 bp contains sequence information for the 5' untranslated region, the signal sequence and the N-terminal portion of gamma-1. Because p γ298 did not encode the C-terminal sequence for mouse anti-CEA gamma 1 chain, plasmid DNA was isolated from other colonies and screened and PstI and NcoI. The C-terminal region of the cDNA insert of Pγ11, one of these isolated, was sequenced and shown to contain the stop codon 3' untranslated sequence and that portion of the coding sequence missing from p γ298.

The nucleotide sequence of the gamma 1 probe includes nucleotides 528 through 542 of the gamma sequence shown in Figure 3 which corresponds perfectly to the first 16 N-terminal amino acids of mature mouse anti-CEA gamma 1 chain (as determined by amino acid sequence analysis of purified mouse anti-CEA gamma 1 chain.). The coding region consists of 57 basepairs or 19 amino acids of presequences and 1346 basepairs or 447 amino acids of mature protein. The mature protein has a variable region of 110 amino acids, a J4 joining region of 13 amino acids and a constant region of 324 amino acids. After the stop codon at amino acid 447 there begins 96 bp of 3' untranslated sequences up to the polyA addition.

### E.1.7 *Construction of a Direct Expression Vector for Mouse Mature Anti-CEA Kappa Chain*

Figure 6 illustrates the construction of the vector for mature mouse anti-CEA kappa chain.

First, an intermediate plasmid pHGH207-1, having a single trp promoter, was prepared as follows:

The 310 bp DNA fragment containing trp promoter was obtained from pF1Ftrp69, described in Goeddel et al., *Nucleic Acids Research* 8: 4057 (1980), incorporated herein by reference, by digestion with EcoRI and inserted into pHGH 107 (described in U.S. Pat. Application No. ) incorporated herein by reference that had been opened with EcoR I, to obtain pHGH 207 which has a double lac promoter followed by the trp promoter, flanked by EcoR I sites. pHGH 207 was digested with Bamh I, followed by partial digestion with EcoRI and the largest fragment which contains the entire trp promoter was isolated. The largest EcoR 1-BamH I fragment was also isolated from pBR322. Both fragments were ligated and the mixture was used to transform *E. coli* 294. $Tet^r$, $Amp^r$ colonies were isolated and most of them had the plasmid with the structure as shown for pHGH207-1.

Plasmid pHGH207-1 is thus a derivative of the plasmid pHGH107 and has the following properties: 1) the human growth hormone gene is flanked by the tryptophan promoter rather than the lac promoter, 2) the plasmid confers ampicillin and tetracycline resistance when expressed in *E. coli*. (See also European Patent Application Publication No. 0036776). A derivative of pHGH207-1 pHGH2076-1 was obtained, which lacks the EcoR I site between the $amp^R$ gene and the trp promoter. This was accomplished by partial digestion of PHGE207-1 with EcoR I, filling in ends with Klenow and dNTPs, and religation to give pHGH207-1*.

5 µg of pHGH207-1* was digested with EcoRI, and the ends extended to blunt ends using 12 units of DNA Polymerase I in a 50 µl reaction containing 60 mM NaCl, 7 mM $MgCl_2$, 7 mM-Tris HCl (pH 7.4) and 1 mM in each dNTP at 37°C for 1 hour, followed by extraction with phenol/$CHCl_3$ and precipitation with ethanol. The precipitated DNA was digested with BamH I, and the large vector fragment purified

using 5 percent polyacrylamide gel electrophoresis, electroelution, phenol/$CHCl_3$ extraction and ethanol precipitation.

The DNA was resuspended in 50 µl of 10 mM Tris pH 8, 1mM EDTA and treated with 500 units Bacterial Alkaline Phosphatase (BAP) for 30' at 65° followed by phenol/$CHCl_3$ extraction and ethanol precipitation.

A partial gene insert was prepared as follows: 7 µg of pK1734 DNA was digested with Pst I and the kappa chain containing cDNA insert was isolated by 6 percent gel electrophoresis, and electoelution. After phenol/$CHCl_3$ extraction, ethanol precipitation and resuspension in water, this fragment was digested with Ava II. The 333 bp Pst I-Ava II DNA fragment was isolated and purified from a 6 percent polyacrylamide gel.

A 15 nucleotide DNA primer was synthesized by the phosphotriester method G. 0. 2,644,432 (supra) (G) and has the following sequence:

Met Asp Ile Val Met

5' ATG GAC ATT GTT ATG 3'

The 5' methionine serves as the initiation codon. 500 ng of this primer was phosphorylated at the 5' end with 10 units T4 DNA kinase in 20 µl reaction containing 0.5 nM ATP. -200 ng of the Pst I-Ava II DNA fragment was mixed with the 20 µl of the phosphorylated primer, heated to 95°C for 3 minutes and quick frozen in a dry-ice ethanol bath. The denatured DNA solution was made 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4), 12 mM in each dNTP and 12 units DNA Polymerase I-Large Fragment was added. After 2 hours incubation at 37°C this primer repair reaction was phenol/$CHCl_3$ extracted, ethanol precipitated, and digested to completion with Sau 3A. The reaction mixture was then electrophoresed on a 6 Percent polyacrylamide gel and -50 ng of the 182 basepair amino-terminal blunt-end to Sau 3A fragment was electroeluted.

The blunt-Sau 3A primer-repair DNA fragment and ~100 ng of the BAP'd partial RI filled in, BamH I fragment from pHGH 207-1* were combined in 20 µl of 20 mM Tris HCl (pH 7.5), 10 mM $MgCl_2$, 10 mM DTT, 2.5 mM ATP and 1 unit of T4 DNA ligase. After overnight ligation at 14°C the reaction was transformed into *E. coli* K12 strain 294. Restriction endonuclease digestion of a number of ampicillin resistant transformants indicated the proper construction and DNA sequence analysis proved the desired nucleotide sequence through the initiation codon of this new plasmid, pKrepair1 (Figure 4).

The remainder coding sequence of the gene insert was prepared as follows:

> The Pst I cDNA insert fragment from 7 µg of K17G4 DNA was partially digested with Ava II and the Ava II cohesive ends were extended to blunt ends in a DNA Polymerase I large fragment reaction. Following 6 percent polyacrylamide gel electrophoresis the 686 basepair Pst I to blunt end Ava II DNA fragment was isolated, purified and subjected to Hpa II restriction endonuclease digestion. The 497 basepair Hpa II to blunt end Ava II DNA fragment was isolated and purified after gel electrophoresis.

10 µg of pKrepair1 DNA was digested with Ava I, extended with DNA polymerase I large fragment, and digested with Xba I. Both the large blunt end Ava I to Xba I vector fragment and the small blunt end Ava I to Xba I fragment were isolated and purified from a 6 percent polyacrylamide gel after electrophoresis. The large vector fragment was treated with Bacterial Alkaline Phoshatase, and the small fragment was digested with Hpa II, electrophoresed on a 6 percent polyacrylamide and the 169 basepair Xba I-Hpa II DNA fragment was purified (Figure E). ~75 ng of the BAP'd XbaI to blunt end Ava I vector DNA fragment, ~50 ng of the blunt ended partial Ava II to Hoa II DNA fragment and

50 ng of the Hpa II-Xba I overnight at 14°, and the reaction mixture transformed into *E. coli* K12 strain 294. Six ampicillin resistant transformants were selected for restrictions endonuclease analysis. One transformant demonstrated the proper construction and was designated pKcea trp 207-1.

E.1.8. *Construction of Direct Expression Vector for Mouse Mature Anti-CEA Gamma 1 Chain.*

Figure 7 illustrates the construction of the expression plasmid for mature mouse anti-CEA gamma 1 chain. This plasmid was constructed in two parts beginning with construction of the C-terminal region of gene. 5 μg of intermediate plasmid pHGH207-1 was digested with Ava I, extended to blunt ends with DNA polymerase I large fragment (Klenow fragment), extracted with phenol/$CHCl_3$, and ethanol precipitated. The DNA was digested with BamH I treated with BAP and the large precipitated fragment was recovered by 6 percent polyacrylamide gel electrophoresis and electroelution.

-5 μg of pγ1 was digested with Pst I and the gamma chain cDNA insert fragment containing the C-terminal portion of the gene was isolated and purified digested with Ava II followed by extension of the Ava II cohesive ends with Klenow and by Taq I digestion. The 375 basepair blunt end Ava II to Taq I fragment was isolated and purified by gel electrophoresis and electroelution.

9 μg of pγ298 was digested with Taq I and BamH I for isolation of the 496 basepair fragment.

Approximately equimolar amounts of the above described three fragments were ligated overnight at 14°, then transformed into *E. coli* strain 294. The DNA from six ampicillin resistant transformants was committed to restriction endonuclease analysis and one plasmid DNA, named pγceatrc, demonstrated the correct construction of the C-terminal potion of gamma 1 (Figure 5).

30 μg of pγ298 was digested with Pst I and the 628 basepair DNA fragment encoding the N-terminal variable region amino acid sequence of mouse anti-CEA gamma chain was isolated and purified. This fragment was further digested with Alu I and Rsa I For isolation of the 280 basepair fragment. A 15 nuclotide DNA primer

met glu val met leu

5' ATG GAA GTG ATG CTG 3'

was synthesized by the phosphotriester method (supra).

The 5' methionine serves as the initiation codon. 500 ng of this synthetic oligomer primer was phosphorylated at the 5' end in a reaction with 10 units T4 DNA kinase containing 0.5 mM ATP.-500 ng of the 280 basepair Ala I Rsa I DNA fragment was mixed with the phosphorylated primer. The mixture was heat denatured for 5 minutes at 95° and quench frozen in dry-ice ethanol. The denatured DNA solution was treated in a manner identical to the kappa chain region reaction except that after 37° incubation and clean up of the reaction the DNA was digested with Hpa II before gel electrophoresis. -50 ng of the expected 125 basepair blunt-end to Hpa II DNA fragment was purified from the gel.

A second aliquot of pγ298 DNA was digested with Pst I and the 628 basepair DNA fragment was isolated from a polyacrylamide gel for further digestion with BamH I and Hpa II. The 380 basepair fragment was isolated and purified from this digest.

-5 μg of pγcearec was digested with EcoR I and the cohesive ends were made flush with Klenow, further digested with BamH I, BAP'd and electrophoresed on a 6 percent polyacrylamide gel. The large vector fragment was isolated and purified.

In a three fragment ligation, the 125 bp blunt-end to Hpa II fragment was combined with -100 ng of the 380 bp BamH I

Hoa II and -100 ng of the BAP'd pγceatro fragment, and ligated overnignt at 4°. *E. coli* K12 strain 294 was transformed with the ligase reaction. The plasmid DNA from 12 ampicillin resistant transformants was analyzed for the correct construction and the nucleotide sequence through the initiation codon was verified for one plasmid DNA, named pγceatrp 207-1.

E.1.9 *Production of Gamma Chain by Cells transformed with Pγceatrp 207-1.*

E.1.10 *Production of Kappa Chain by Cells Transformed with pKceatrp 207-1.*

E.1.11 *Reconstitution of Antibody from Recombinant K and Gamma Chains*

E.2 *Assay Method*

E.3 *Preparation of Hybrid Antibody*

E.4 *Preparation of Fab*

E.4.1 *Construction of Mouse Anti-CEA Gamma 1 Fab Fragment Vector*

Figure 3 presents the construction of an expression vector for mouse anti-CEA gamma 1 Fab fragment. 5 μg of pBR322 was digested with Hind III, the cohesive ends made flush by filling in using Klenow enzyme; digested with Pst I, BAP'd and electrophoresed through a 6 percent polyacrylamide gel. The large vector fragment was isolated and purified from the gel.

5 μg of pγceatrp207-1* was digested with both BamH I and Pst I and the -1570 bp DNA fragment containing the trp promoter and the gene sequence encoding the variable region continuing into constant region and further into the anti-CEA gamma 1 chain hinge region, was isolated and purified after electrophoresis.

Expression of the anti-CEA gamma 1 chain Fab fragment requires that a termination codon be constructed at the C-terminus of the gene. For this, the 260 bp Nce I to Nde I DNA fragment from 20 μg of the pγ298 was isolated and purified. A 13 nucleotide DNA primer, the complement of which encodes the last 3 C-terminal amino acids of the Fab gene and 2 bases of the 3 needed for the stop codon, synthesized by the phosphotriester method (supra) and has the following sequence:

AspCysGlyStop

3' CCCTAAACACCAAC 5'

The third base of the stop codon is provided by the terminal nucleotide of the filled-in Hind III site op cit. 500 ng of this primer was used in a primer repair reaction with -200 ng of the Nco I Nde I DNA fragment. The DNA was then digested with BamH I and the reaction electrophoresed through a 6 percent polyacrylamide gel. -50 ng of the 181 bp blunt end to BamH I DNA fragment was isolated and purified.

-100 ng of the BAP'd filled-in Hind III-Pst I vector fragment, -100 ng of the BamH I Pst I fragment and the 181 basepair blunt end to BamH I repair fragment was ligated overnight and transformed into *E. coli* K12 strain 294. Plasmid DNA from several tetracycline resistant transformants was analyzed for the proper construction and the nucleotide sequence through the repair blunt end filled-in Hind III junction was determined for verification of the 5' TGA stop codon.

E.4.2 *Expression of Gene for Gamma Fab Fragment*

*Claims*

1. Antibodies produced by recombinant host cells.
2. Antibodies substantially free of other proteins of mammalian origin.

3. The antibodies of Claim 1 or 2 which are mammalian antibodies in that the amino acid sequences of all four chains are homologous to the sequences in the corresponding chains in antibodies derived from a mammalian species.

4. The antibodies of Claim 3 wherein the mammalian species is murine.

5. The antibodies of Claim 3 wherein the mammalian species is human.

6. The antibodies of Claim 1 or 2 which are composite antibodies.

7. The antibodies of Claim 6 which are divalent antibodies.

8. The antibodies of Claim 6 wherein the amino acid sequences of one pair of heavy and light chain is homologous to the corresponding amino acid sequences of the antibodies raised in response to a first antigen species, and the amino acid sequences of the other pair of heavy and light chain is homologous to the corresponding amino acid sequences of antibodies raised in response to a second, different, antigen.

9. The antibodies of Claim 6 or 7 wherein the homology of the heavy chains corresponds to murine antibodies, and the homology of the light chains corresponds to human antibodies.

10. The antibodies of Claim 1 or 2 which are hybrid antibodies.

11. The antibodies of Claim 10 wherein the constant regions of all four chains are homologous to the corresponding constant regions of antibodies of a first mammalian species, and the amino acid sequence of the variable regions of all four chains are homologous to the variable regions in antibodies derived from a second, different, mammalian species.

12. The antibodies of Claim 11 wherein the homology of the constant regions corresponds to murine antibodies and the homology of the variable region corresponds to human antibodies.

13. The antibodies of Claims 1, 2, 3, 6, or 10 which are antigenic against CEA.

14. The antibodies of Claims 1, 2, 3, 6, or 10 wherein the heavy chain is of the gamma family.

15. The antibodies of Claims 1, 2, 3, 6, or 10 wherein the light chain is of the kappa family.

16. A composition of matter consisting essentially of Fab region.

17. The composition of matter of Claim 16 which is produced by recombinant host cells.

18. The composition of matter of Claim 17 which is Mammalian Fab region.

19. The composition of matter of Claim 17 which is a divalent Fab region.

20. The composition of matter of Claim 17 which is a hybrid Fab region.

21. The composition of matter of Claim 20 wherein the amino acid sequence of the variable region wherein the amino acid sequences of the variable region of both chains is homologous to corresponding sequences of antibodies derived from a first mammalian species, and the amino acid sequences of the constant regions of both chains are homologous to the corresponding amino acid sequences of antibodies derived a second, different mammalian species.

22. The composition of matter of claims 16 through 20 wherein the composition of matter is immunoreactive against CEA.

23. A sequence of amino acids produced by recombinant host cells corresponding to the heavy chain of antibody.

24. The sequence of Claim 23 which is a mammalian heavy chain.

25. The sequence of Claim 24 which is homologous to the heavy chain of a human or murine antibody.

26. The sequence of Claim 23 which is a hybrid heavy chain.

27. The sequence of Claim 26 wherein that portion of the sequence which corresponds to the variable region is homologous to corresponding sequences of antibodies derived from a first mammalian species, and the amino acid sequences of the constant regions of both chains are homologous to the corresponding amino acid sequences of antibodies derived a second, different mammalian species.

28. The sequence of Claim 23 through 27 which corresponds to the sequences of the gamma family.

29. A sequence of amino acids produced by recombinant host cells corresponding to the light chain of a mammalian antibody.

30. The sequence of Claim 29 which is a mammalian light chain.

31. The sequence of Claim 30 which is homologous to the light chain of a murine or human antibody.

32. The sequence of Claim 29 which is a hybrid light chain.

33. The sequence of Claim 32 wherein that portion of the sequence which corresponds to the variable region is homologous to corresponding sequences of antibodies derived from a first mammalian species, and the

amino acid sequences of the constant regions of both chains are homologous to the corresponding amino acid sequences of antibodies derived a second, different mammalian species.

34. The amino acid sequence of Claims 29 through 33 which corresponds to the sequence of the kappa family.

35. A DNA sequence which codes for the antibody of Claims 1, 2, 3, 6, or 10.

36. A replicable expression vector capable of expressing in a suitable host cell the DNA sequence of Claim 35.

37. An expression plasmid which comprises the DNA sequence of Claim 35 operably linked to a promoter compatible with a suitable host cell.

38. A DNA sequence which encodes for the composition of matter of Claim 16 or 17.

39. A replicable expression vector capable of expressing in a suitable host cell the DNA sequence of Claim 38.

40. An expression plasmid which comprises the DNA sequence of Claim 38 operably linked to a promoter compatible with a suitable host cell.

41. A DNA sequence which codes for the amino acid sequence of Claim 23.

42. A replicable expression vector capable of expressing in a suitable host cell the DNA sequence of Claim 41.

43. An expression plasmid which comprises the DNA sequence of Claim 41 operably linked to a promoter compatible with a suitable host cell.

44. A DNA sequence which encodes the amino acid sequence of Claim 29.

45. A replicable expression vector capable of expressing in a suitable host cell the DNA sequence of Claim 44.

46. An expression plasmid which comprises the DNA sequence of Claim 44 operably linked to a promoter compatible with a suitable host cell.

47. Recombinant host cells or host cell cultures transformed with the vector of Claim 36 or 37.

48. Recombinant host cells or host cell cultures transformed with the vector of Claim 39 or 40.

49. Recombinant host cells or host cell cultures transformed with the vector of Claim 42 or 43.

50. Recombinant host cells or host cell cultures transformed with the vector of Claim 45 or 46.

51. A method for reconstituting antibody heavy and light chains, which method comprises treating an approximately equimolar mixture of such chains with a mild denaturant in the presence of a reducing agent, followed by dialysis into dilute buffer in the presence of air.

52. The method of Claim 51 wherein heavy and light chains are derived from recombinant host cell culture.

53. A method for preparing antibodies in recombinant host cells which method comprises

    a) preparing a DNA sequence encoding heavy chain,

    b) inserting the sequence of a) into a replicable expression vector operably linked to a suitable promoter,

    c) preparing a DNA sequence encoding light chain,

    d) inserting the sequence of c) into a replicable expression vector operably linked to a suitable promoter,

    e) transforming host cell culture with the vector of b) and host cell culture with the vector of d),

f) recovering light chain and heavy chain from cell culture,

g) reconstituting light and heavy chain.

54. The method of Claim 53 wherein the vector of b) and the vector of d) are used to transform the same host cell culture.

55. The method of Claim 54 wherein the sequence of a) and the sequence of a) are inserted into the same replicable expression vector.

56. The method of Clam 53 wherein the DNA sequence of a) encodes mammalian heavy chain, and the DNA sequence of c) encodes mammalian light chain; and wherein both DNA fragments encode amino acid sequences of the same mammalian antibody.

57. The method of Claim 53 wherein the DNA sequence in a) encodes a mammalian heavy chain, the DNA sequence in b) encodes mammalian light chain, and wherein the DNA fragments of light and heavy chain encode for amino acid sequences which correspond to sequences from different mammalian antibodies.

58. The method of Claim 53 wherein the DNA fragment of a) encodes hybrid heavy chain and the DNA sequence of c) encodes hybrid light chain.

59. A method for preparing Fab region in recombinant host cells which method comprises

a) preparing a DNA sequence encoding the Fab region of heavy chain

b) inserting the sequence of a) into a replicable expression vector operably linked to a suitable promoter,

c) preparing a DNA sequence encoding light chain.

d) inserting the sequence of b) into a replicable expression vector operably linked to a suitable promoter,

e) transforming host cell culture with the vector of B and host cell culture with the vector of D,

f) recovering light chain and Fab region of heavy chain from cell culture,

g) reconstituting light and heavy Fab region chains.

60. The method of Claim 59 wherein the DNA sequence in a) encodes a mammalian heavy chain Fab region and the DNA sequence in c) encodes a mammalian light chain.

61. The method of Claim 59 wherein the DNA sequence in a) encodes a mammalian Fab region of heavy chain corresponding to Fab of one mammalian antibody, and the DNA sequence in c) encodes for light chain of another mammalian antibody.

62. The method of Claim 59 wherein the DNA sequence in a) encodes hybrid Fab region of a heavy chain, and the DNA sequence in c) encodes a hybrid light chain.

63. A method for preparing antibody heavy chain which method comprises preparing

a) a DNA sequence encoding heavy chain,

b) inserting said sequence into a replicable expression vector operably linked to a suitable promoter,

c) transforming host cell culture with the vector of b) and

d) recovering heavy chain from cell culture.

64. A method for preparing antibody light chain which method comprises preparing

a) a DNA sequence encoding light chain,

b) inserting said sequence into a replicable expression vector operably linked to a suitable promoter,

c) transforming host cell culture with the vector of b),

d) recovering light chain from cell culture.

65. A method for preparing antibody Fab region which method comprises preparing

a) a DNA sequence encoding Fab region,

b) inserting said sequence into a replicable expression vector operably linked to a suitable promoter,

c) transforming host cell culture with the vector of b),

d) recovering Fab region from cell culture.

[*Exhibit 3 to Winters Declaration*]

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

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No. C98-3926 MMC ENE

---

GENENTECH, INC.

*Plaintiff,*

vs.

CELLTECH THERAPEUTICS, LTD.,

*Defendant.*

---

DEPOSITION UPON ORAL EXAMINATION OF
DOCTOR SHMUEL CABILLY

Volume II
(Pages 165-322)

On Wednesday, 2nd February 2000
Commencing at 9:15 a.m.

Taken at the offices of
Morrison & Foerster
21 Garlick Hill
London EC4, England.

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Reported by Alan J. Bell, MBIVR, MNCRA

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* * *

[275] A. It is a fact that I prepared them from them. I do not remember, apart from this case, that I gave other people cotransformed cells, right now.

Q. Other than this instance where you gave samples to Jeanne Perry, do you remember any other instance where you gave samples derived from cotransformed cells?

MR. WINTERS: Same objection.

THE WITNESS: I cannot remember, no.

BY MR. KREEGER:

Q. Do you have any financial interest in royalties or otherwise associated with if Genentech prevails and gets a patent in this case?

A. Not that I know right now.

MR. WINTERS: I am sorry, objection: vague; may call for a legal conclusion. You can answer.

THE WITNESS: Not that I know right now.

(Exhibit 101 was marked for identification)

BY MR. KREEGER:

Q. I am showing you what has been marked as Exhibit 101 and I ask if you recognize [276] this document.

A. Yes.

Q. At one point in your deposition you mentioned having found a draft of the patent application. Is this the patent application that was recently found?

MR. WINTERS: It is vague, but—

MR. KREEGER: I am sorry, I did not mean to interrupt you.

A. I think that a copy of this one I saw before. Now, this copy was in my possession, OK.

Q. This was in your possession, Exhibit 101?

A. Yes.

Q. There was another draft that was in your possession. Is that right?

A. Yes.

(Exhibits 102 and 103 were marked for identification)

MR. WINTERS: I am sorry, I am going to object, because you are calling two moves that have busted me. Apparently there is a local rule [277] about not marking as exhibits parts of the same document. 102, and I think what you have marked as 103, were produced together.

MR. KREEGER: OK. In the version that we were produced, they were not literally affixed to one another. I was just about to ask him if they were part of the same document.

MR. WINTERS: Fine.

BY MR. KREEGER:

Q. When you found these in your files, was the cover letter attached to the draft that is sitting next to it?

A. Can I see it first?

Q. You may.

A. Because this is a different—

Q. Please.

MR. FITTON: They were not attached.

MR. WINTERS: By "attached" do you mean affixed or attached do you mean a part of?

BY MR. KREEGER:

Q. I mean attached to one another, affixed.

A. In my folder they were one above the other one.

[278] Q. Just so the record is clear, the one-page document that I have marked as Exhibit 103 was sitting on top of the document that we have marked as Exhibit 102?

A. Yes.

Q. Sitting here today, do you know if you received Exhibit 103 and Exhibit 102 together?

A. I assume I received them, I think that I received them, together.

Q. There is some marking on Exhibit 102?

A. OK.

Q. Are those your marks?

MR. WINTERS: Would you like the original?

THE WITNESS: I would prefer to look at the original.

MR. KREEGER: The witness is now looking at the original of the same document.

A. Some of them; some of them, yes.

Q. Some of the marking is not yours?

A. Some of them are not.

Q. The marks that were not yours; were they present when you received the draft patent [279] application?

MR. WINTERS: Do you understand the question?

A. Yes, I understand. No. No, to the best of my ability to judge, they came clean.

BY MR. KREEGER:

Q. Can you tell whose marking is on there other than yours?

A. It seems Art's, Art Riggs.

Q. Could you indicate which are the pages that have Dr. Riggs' writing on them?

A. Yes.

MR. WINTERS: By that it may be that both Dr. Riggs and Dr. Cabilly wrote on them, but you want those pages in which some or all of the handwriting is Dr. Riggs'?

MR. KREEGER: Right.

A. The first page contains Dr. Riggs.

Q. He wrote the "revertebrate"?

A. Yes, and the upper part. Page number 2 also, some of them are of Dr. Riggs.

Q. Which of those are Dr. Riggs?

A. You can tell by the handwriting, line 3 it is Dr. Riggs. Then in the middle of the [280] first paragraph, we have "the resulting genome" and above it you will see Dr. Riggs' handwriting.

MR. WINTERS: Is there a way to tell, pen or pencil? Can I just suggest that question is a way to differentiate between his and Riggs.

BY MR. KREEGER:

Q. My photocopy does not make that clear. Can you tell?

A. No, because this is pencil and this is my handwriting.

MR. WINTERS: OK, I did not know. I just thought it might make it quicker.

BY MR. KREEGER:

Q. Is it mostly Riggs?

A. No, you see some of the references there are mine.

Q. The parentheses and the numbers?

A. Yes, they are mine. This, on page 3, you have "myeloma" and the references are mine. Page 4 is my handwriting. Page 5, this is my handwriting at the middle of it. Then, further on, page 9 is Art Riggs' handwriting. Page 22, that is my handwriting. Page 33 it is not my [281] handwriting. Page 35, at the bottom, it is Art Riggs' handwriting. And that is it.

Q. Do you know when it was that you received the draft patent application, Exhibit 102?

A. In terms of what, years, month, days, hours?

Q. I think you will see the cover letter is dated February 25th 1983 and I was wondering if you knew when it was that you actually received it?

A. Right now, I cannot tell you.

Q. What about the draft that is marked as Exhibit 101. Do you know when you received that draft? First of all, I take it that Exhibit 101 also came from your files, or is that not true?

A. Yes, it came from my files. This is 101?

Q. 101, yes. Why do you not look at the exhibit here.

A. OK.

Q. This one also came from your files?

A. Yes.

Q. You received Exhibit 101 after you received Exhibit 102?

[320] A. I did not ask; I do not know.

MR. WINTERS: So the record is clear, I think the answer to that is "Yes".

My understanding is yes, that Genentech thinks it is appropriate—given Dr. Cabilly's extremely impacted schedule and where he is in his life—to compensate him for his time and they are doing it.

THE WITNESS: Now I thank you!

MR. KREEGER: I am through. Thank you very much.

(The deposition concluded at 2.42 p.m.)

[*Exhibit 12 to Winters Declaration*]

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

---

No. C-98-3926

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GENENTECH, INC.

*Plaintiff,*

vs.

CELLTECH LIMITED,

*Defendant.*

---

REPORTER'S TRANSCRIPT OF PROCEEDINGS
BEFORE THE HONORABLE MAXINE M. CHESNEY
UNITED STATES DISTRICT JUDGE
JULY 28, 2000

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APPEARANCES:

FOR THE PLAINTIFF: GENENTECH INCORPORATED
LATHAM & WATKINS
BY: VERNON WINTERS, Esq.
135 Commonwealth Drive
Menlo Park, CA 94025

[2] LATHAM & WATKINS
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505 Montgomery St. #1900
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FOR THE DEFENDANT: CELLTECH LIMITED
MORRISON & FOERSTER
BY: MATTHEW KREEGER, Esq.
BY: TAMU K. SUDDUTH, Esq.
425 Market Street
San Francisco, CA 94105

* * *

[91] MR. KREEGER: And the Court may have questions as well.

MR. WINTERS: Of course.

THE COURT: I may well. Also I think that there are ways that you can narrow some of the testimony certainly with respect to the qualifications of the witnesses. You can maybe highlight a couple of noble [*sic*] prizes or something and go on, you know.

You don't have to give me every paper they wrote and then every school they attended and just maybe highlight a couple of things that are particularly impressive.

All of these people respect each other and that suggest [*sic*] that they're all qualified and impressive people in their own right.

I would like to take up a housekeeping matter as well. We talked at the last calling of the case which was a case management conference about whether there was any possibility the case resolving by way of agreement as opposed to full [92] litigation of which it's going to be long, expensive and won't even be the end, as I understand it, this can go up after I rule, correct?

MR. WINTERS: Yes.

MR. KREEGER: Yes.

THE COURT: So you know I don't want to just characterize myself as a waste [*sic*] station but given the fact that your clients have so much apparently at steak [*sic*] and so con-

cerned about the matter, I'd be hard pressed to see whoever does not prevail, doesn't want to go further with the matter.

So that if you're really trying to resolve it and have some type of a completion of this matter within some reasonable period of time, and I guess more than a reasonable amount has already gone on, but from this point I was encouraging you to, at least, see about the potential ADR. And you told me I believe that the choice would be private mediation.

MR. WINTERS: Yeah.

MR. KREEGER: Yes.

THE COURT: Have you set something up?

MR. WINTERS: We haven't. We've [93] discussed with a retired Judge Lynch. Genentech had used before and been happy with that performance.

We're willing to take that to mediation, set a date for that.

THE COURT: You have?

MR. WINTERS: Yeah. We haven't set that up. The Court set a date. Looks like we may have a mediator preference between the parties so I expect early next week we'll try to get that going.

THE COURT: I would hope you would agree on a mediator. Judge Lynch, as you know, was a member of this bench and conducted a reduced-rate settlement conference to witness mediations here on the bench, but he has left the bench.

MR. .WINTERS: Increased his rate.

MR. KREEGER: I have no doubt we'll find an agreement.

THE COURT: You need to get going on that.

MR. WINTERS: Very well.

THE COURT: Because this is not something that you can just pop in for a couple of minutes and then it's all over.

I think if you're going to admit [94] yourself to actually engaging in the process, you really have to put your full effort into it. So the sooner you get that scheduled the better.

* * *

[*Exhibit 15 to Winters Declaration*]

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

---

CASE NO. C98-3926 MMC (WDB)

---

GENENTECH, INC.,

*Plaintiff,*

v.

CELLTECH THERAPEUTICS, LTD.,

*Defendant.*

---

NOTICE OF SETTLEMENT AND JOINT REQUEST FOR ENTRY OF SETTLEMENT INSTRUMENTS

This Notice Relates to a Status Conference Scheduled for March 9, 2001 at 10:30 A.M.

The Parties have reached a settlement of this matter and all settlements documents have been duly executed. As part of the settlement, the Parties have agreed that an Order and Judgment should issue from this Court, the effect of which will be to order the Patent and Trademark Office (PTO) to (i) vacate the decision in *Cabilly, et al. v. Boss et al.*, Patent Interference No. 102,572, (ii) revoke and vacate United States Patent No. 4,816,397, issued March 28, 1989 (the Celltech Patent), and (iii) grant and issue a United States patent based upon pending United States Patent Application No. 07/215,419, such patent having those claims 101-120 that were allowed by the PTO in such pending patent application (the Genentech Patent). The Parties' settlement is conditioned upon the Court issuing the Order and the Judgment and upon the PTO taking the prescribed actions.

The proposed Judgment and Order (two separate documents) are being filed herewith. The Judgment is the

document which directs the PTO to take certain actions and retains jurisdiction to ensure such actions are taken. The Order contains findings of fact related to the judgment, vacates certain prior orders, and provides for the return of documents filed under seal. The Parties jointly request the Court to enter both the Judgment and the Order.

While the Parties believe the Judgment and Order are self-explanatory, the stand ready to provide, through whatever means the Court desires, additional explanation or argument in support of the entry of such instruments. As discussed at the February 16, 2001, telephonic status conference, the Parties stand ready to attend the March 9, 2001, telephonic status conference unless they are advised by the courtroom deputy that their attendance is not necessary.

Dated: March 6, 2001

Respectfully submitted,

LATHAM & WATKINS

By /s/ Daniel Wall by Rachel Krevans by permission
DANIEL M. WALL
Attorneys for GENENTECH, INC.

Dated: March 6, 2001

Respectfully submitted,

MORRISON & FOERSTER

By /s/ Rachel Krevans
RACHEL KREVANS
Attorneys for CELLTECH
THERAPEUTICS, LTD.

[*Exhibit 16 to Winters Declaration*]

[Proposed Order]

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

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CASE NO. C98-3926 MMC

---

GENENTECH, INC.,

*Plaintiff,*

v.

CELLTECH THERAPEUTICS, LTD.,

*Defendant.*

---

[Proposed] Order Regarding Resolution of Interference

The Court hereby makes the following orders in this case:

[Proposed] Findings of fact and conclusions of law

1. Plaintiff, Genentech, Inc. filed this action under 35 U.S.C. § 146, following a decision in Patent Interference No. 102,572 before the Board of Patent Appeals and Interferences ("Board") of the United States Patent and Trademark Office ("PTO"). In that decision the Board concluded that Michael A. Boss, John H. Kenten, John S. Emtage and Clive R. Wood (collectively "Celltech Inventors") were entitled to priority over Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur .D. Riggs, and Ronald B. Wetzel (collectively "Genentech's inventors") with respect to the invention defined by the interference count, which corresponded to claims 1-18 of U.S. Patent No. 4,816,397 ("the Boss patent"), issued to Celltech's inventors and assigned to Celltech.

2. The invention at issue relates to a process for producing genetically engineered immunologically functional antibodies, also referred to as immunoglobulin ("Ig") molecules. Immunologically functional Ig molecules (i.e., Ig molecules capable of binding with their associated antigen at levels above background) have a variety of potential uses including use as reagents in laboratory procedures and as therapeutic agents.

3. In the early 1980s, both Genentech and Celltech studied the use of recombinant DNA technology to produce Ig molecules. At roughly the same time, both developed the means to create immunologically functional Ig molecules. The dispute in this case is who first satisfied the requirements of the United States patent laws with regards to conception, and thus who had priority to the patent. In particular, the dispute centers on who first "conceived" the means to produce immunologically functional Ig molecules. The patent laws define "conception" as the purely mental act occurring when the inventor forms a definite and permanent idea of the complete and operative invention, such that one of ordinary skill could reduce the invention to practice without extensive research or experimentation. The date of conception must be corroborated by evidence other than the inventor's testimony, such as laboratory notebooks, patent applications or drafts, or other documentary evidence.

4. Celltech claims a priority date of March 25, 1983, the date it filed a British patent application describing the invention, and therefore proving conception. Accordingly, in order for Genentech to establish priority, it must prove and corroborate a conception prior to March 25, 1983.

5. Genentech filed its U.S. patent application on April 8. 1983 and Celltech filed its U.S. patent application in November 14, 1984. On March 28, 1989, part of Genentech's application issued as U.S. Patent No. 4,816,517, "Recombinant Immunoglobulin Preparations," and Celltech's application also issued as U.S. Patent No. 4,816,397, "Multichain Polypeptides or Proteins and Processes for their Production." Thereafter, Genentech amended a pending continuation of its application to copy exactly the claim in Celltech's patent, the permitted and standard procedure for provoking an interference.

6. On February 28, 1991, the PTO's Board of Patent Appeals and Interferences declared an interference between Celltech's patent and Genentech's continuation application. Genentech was originally named the senior party to the interference on account of its earlier U.S. filing date. However, Celltech thereafter filed a motion to be named the senior party, arguing that its priority British patent application corroborated a complete conception of the invention before Genentech first filed its U.S. patent application. That motion was granted, and ultimately the PTO concluded that because Genentech failed to prove a conception earlier than March 28, 1983, Celltech was entitled to priority.

7. Genentech commenced this action on October 9, 1998. Discovery ensued and was completed. During the course of discovery, additional evidence of Genentech research on immunologically functional Ig molecules was uncovered, including a draft of what became Genentech's U.S. patent application, which draft is dated February 25, 1983—a month before Celltech failed its British patent application. The PTO did not consider this draft patent application.

8. It is undisputed that if this draft is sufficient to corroborate conception of the invention as of February 25, 1983, Genentech is entitled to priority. Celltech does not claim any basis for an earlier priority date.

9. Genentech's February 25, 1983 draft patent application is sufficient to corroborate Genentech's complete conception of the invention by that date. The description of the invention contained in the draft shows that Genentech's inventors had formed, by February 25, 1983, a definite and permanent idea of the complete and operative invention, such that one of ordinary skill could reduce the invention to practice without extensive research or experimentation. Furthermore, the description of the invention contained in Genentech's draft is at least equivalent to the description contained in Celltech's British application, upon which the PTO relied in concluding that Celltech was entitled to priority

10. Accordingly, the Court finds and rules that Genentech is entitled as a matter of law to priority over Celltech to the invention described by the count.

Vacating of prior Orders

The Court hereby vacates the following prior Orders in this case:

1. The Orders of Magistrate Judge Wayne D. Brazil dated January 14, 2000.

2. This Court's Order dated February 17, 2000 denying Genentech's appeal of Magistrate Judge Brazil's January 14, 2000 Order.

3. This Court's Order dated July 31, 2000 denying plaintiff Genentech Inc.'s summary adjudication and count construction motions.

Documents filed under seal

1. In addition, the Court hereby directs the Clerk of the Court to allow counsel for the parties to remove from the court's files all documents filed under seal in this case. As those documents were filed under seal, they did not become part of the public record in this case.

IT IS SO ORDERED.

Dated: March __, 2001.

By_____
United States District Judge

[*Exhibit 17 to Winters Declaration*]

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

CASE NO. C98-3926 MMC

GENENTECH, INC.,

*Plaintiff*,

v.

CELLTECH THERAPEUTICS, LTD.,

*Defendant*.

[Proposed] Judgment

Plaintiff, Genentech, Inc., filed this action under 35 U.S.C. § 146 following a decision in Patent Interference No. 102,572 before the Board of Patent Appeals and Interferences ("Board") of the United States Patent and Trademark Office ("PTO"). In that decision, the Board concluded that Michael A. Boss, John H. Kenten, John S. Emtage, and Clive R. Wood (collectively "Celltech's inventors") were entitled to priority over Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel (collectively "Genentech's inventors") with respect to the invention defined by the interference count, which corresponded to claims 1-18 of issued US Patent No. 4,816,397.

Pursuant to Rule 54(b) of the Federal Rules of Civil Procedure, the Court orders and adjudges that the following shall occur simultaneously:

1. The Court directs the PTO to vacate the PTO's decision in *Cabilly, et al v. Boss, et al.*, Patent Interference No. 102, 572.

2. The Court directs the PTO to revoke and vacate United States Patent No. 4,816,397, issued March 28, 1989 to Boss, *et al.*;

3. The Court directs the PTO to grant and issue to Genentech's Inventors with Genentech as the assignee), with the issue date being the same as the date of revocation of United States Patent No. 4,816,397, a United States patent having those claims 101-120 that were allowed by the PTO in Genentech's pending United States Patent Application No. 07/205,419, which is a continuation of Genentech's United States Application No. 06/483,457, filed April 8, 1983.

The Court shall retain jurisdiction over this matter pending the PTO's compliance with the above orders and this Judgment. If for any reason the PTO does not comply with the orders set out above, then these orders, this Judgment, and the Order regarding resolution of the interference shall be vacated, and shall have no force and effect, and shall not be relied upon by any person for any purpose, and Genentech and Celltech shall promptly proceed to arbitration as provided in the Settlement Negotiation and Alternative Dispute Resolution Agreement between Genentech and Celltech dated September 18, 2000.

The parties shall bear their own respective attorneys' fees and costs.

IT IS SO ADJUDGED.

Dated: March __, 2001.

By _____
United States District Judge

[*Exhibit 18 to Winters Declaration*]

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

[Filed March 16, 2001]

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Case No. C98-3926 MMC (WDB)

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GENENTECH, INC.,

*Plaintiff,*

vs.

CELLTECH THERAPEUTICS, LTD.,

*Defendant.*

---

Order Regarding Resolution of Interference

Pursuant to the settlement agreement between the parties, the Court hereby makes the following orders in this case:

Findings of fact and conclusions of law

1. Plaintiff, Genentech, Inc., filed this action under 35 U.S.C. § 146, following a decision in Patent Interference No. 102,572 before the Board of Patent Appeals and Interferences ("Board") of the United States Patent and Trademark Office ("PTO"). In that decision, the Board concluded that Michael A. Boss, John H. Kenten, John S. Emtage, and Clive R. Wood (collectively "Celltech's inventors") were entitled to priority over Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel (collectively "Genentech's inventors") with respect to the invention defined by the interference count, which corresponded to claims 1-18 of U.S. Patent No. 4,816,397 ("the Boss patent"), issued to Celltech's inventors and assigned to Celltech.

2. The invention at issue relates to a process for producing genetically engineered immunologically functional antibodies, also referred to as immunoglobulin ("Ig") molecules immunologically functional Ig molecules (i.e., Ig molecules capable of binding with their associated antigen at levels above background) have a variety of potential uses, including use as reagents in laboratory procedures and as therapeutic agents.

3. In the early 1980's, both Genentech and Celltech studied the use of recombinant DNA technology to produce Ig molecules. At roughly the same time, both developed the means to create immunologically functional Ig molecules. The dispute in this case is who first satisfied the requirements of the United States patent laws with regards to conception, and thus who had priority to the patent. In particular, the dispute centers on who first "conceived" the means to produce immunologically functional Ig molecules. The patent laws define "conception" as the purely mental act occurring when the inventor forms a definite and permanent idea of the complete and operative invention, such that one of ordinary skill could reduce the invention to practice without extensive research or experimentation. The date of conception must be corroborated by evidence other than the inventor's testimony, such as laboratory notebooks, patent applications or drafts, or other documentary evidence.

4. Celltech claims a priority date of March 25, 1983, the date it filed a British patent application describing the invention, and therefore proving conception. Accordingly, in order for Genentech to establish a priority, it must prove and corroborate a conception prior to March 25, 1983.

5. Genentech filed its U.S. patent application on April 8, 1983 and Celltech filed its U.S. patent application in November 14, 1984. On March 28, 1989, part of Genentech's application issue as U.S. Patent No. 4,816,517, "Recombinant immunoglobulin Preparations," and Celltech's application

also issued as U.S. Patent No. 4,816,397, "Multichain Polypeptides or Proteins and Processes for their Production." Thereafter, Genentech amended a pending continuation of its application to copy exactly the claim in Celltech's patent, the permitted and standard procedure for provoking an interference.

6. On February 28, 1991, the PTO's Board of Patent Appeals and Interferences declared an interference between Celltech's patent and Genentech's continuation application. Genentech was originally named the senior party to the interference, on account of its earlier U.S. filing date. However, Celltech thereafter filed a motion to be named the senior party, arguing that its priority British patent application corroborated a complete conception of the invention before Genentech first filed its U.S. patent application. That motion was granted, and ultimately the PTO concluded that because Genentech failed to prove a conception earlier than March 28, 1983, Celltech was entitled to priority.

7. Genentech commenced this action on October 9, 1998. Discovery ensued and was completed. During the course of discovery, additional evidence of Genentech's research on immunologically functional Ig molecules was uncovered, including a draft of what became Genentech's U.S. patent application, which draft is dated February 25, 1983—a month before Celltech filed its British patent application. The PTO did not consider this draft patent application.

8. It is undisputed that if this draft is sufficient to corroborate conception of the invention as of February 25, 1983, Genentech is entitled to priority. Celltech does not claim any basis for an earlier priority date.

9. Genentech's February 25, 1983 draft patent application is sufficient to corroborate Genentech's complete conception of the invention by that date. The description of the invention contained in the draft shows that Genentech's inventors had formed, by February 25, 1983, a definite and

permanent idea of the complete and operative invention, such that one of ordinary skill could reduce the invention to practice without extensive research or experimentation. Furthermore, the description of the invention contained in Genentech's draft is at least equivalent to the description contained in Celltech's British application, upon which the PTO relied in concluding that Celltech was entitled to priority.

10. Accordingly, the Court finds and rules that Genentech is entitled as a matter of law to priority over Celltech to the invention described by the count.

Vacating of prior Orders

The Court hereby vacates the following prior Orders in this case:

1. The Order of Magistrate Judge Wayne D. Brazil dated January 14, 2000.

2. This Court's Order dated February 17, 2000 denying Genentech's appeal of Magistrate Judge Brazil's January 14, 2000 Order.

3. This Court's Order dated July 31, 2000 denying plaintiff Genentech, Inc.'s summary adjudication and count construction motions.

Documents filed under seal

1. In addition, the Court hereby directs the Clerk of the Court to allow counsel for the parties to remove from the courts files all documents filed under seal in this case. As those documents were filed under seal, they did not become part of the public record in this case.

IT IS SO ORDERED

Dated: March 16, 2001

By: /s/ Maxine M. Chesney
United States District Judge

[*Exhibit 19 to Winters Declaration*]

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

[Filed March 16, 2001]

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Case No. C98-3926 MMC (WDB)

---

GENENTECH, INC.,

*Plaintiff,*

vs.

CELLTECH THERAPEUTICS, LTD.,

*Defendant.*

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Judgment

1. Plaintiff, Genentech, Inc., filed this action under 35 U.S.C. § 146, following a decision in Patent Interference No. 102,572 before the Board of Patent Appeals and Interferences ("Board") of the United States Patent and Trademark Office ("PTO"). In that decision, the Board concluded that Michael A. Boss, John H. Kenten, John S. Emtage, and Clive R. Wood (collectively "Celltech's inventors") were entitled to priority over Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel (collectively "Genentech's inventors") with respect to the invention defined by the interference count, which corresponded to claims 1-18 of U.S. Patent No. 4,816,397.

Pursuant to the settlement agreement between the parties, and pursuant to Rule 54(b) of the Federal Rules of Civil Procedure, the Court orders and adjudges that the following shall occur simultaneously:

1. The Court directs the PTO to vacate the PTO's decision in *Cabilly, et al. v. Boss, et al.*, Patent Interference No. 102,572.

2. The Court directs the PTO to revoke and vacate United States Patent No. 4,816,397, issued March 28, 1989 to *Boss, et al.*

3. The Court directs the PTO to grant and issue to Genentech inventors (with Genentech as the assignee), with the issue date being the same of revocation of the United Sates Patent No. 4,816,397, a United States patent having thoses claims 101-120 that were allowed by the PTO in Genentech's pending United States Patent Application No. 07/205,419, which is a continuation of Genentech's United States Patent Application No. 06/483,457 filed April 8, 1983.

The Court shall retain jurisdiction over this matter pending the PTO's compliance with the above orders and judgment. If for any reason the PTO does not comply with the orders set out above, then those orders, this Judgment, and the Order regarding resolution of the interference shall be vacated, and shall have no force and effect, and shall not be relied upon by any person for any purpose, and Genentech and Celltech shall promptly proceed to arbitration as provided in the Settlement Negotiation and Alternative Dispute Resolution Agreement between Genentech and Celltech dated September 18, 2000.

The parties shall bear their own respective attorneys' fees and costs.

IT IS SO ADJUDGED

Dated: March 16, 2001

By: /s/ Maxine M. Chesney
United States District Judge

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Jan. 14, 2004]

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Case No. CV 03-2567 MRP

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MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

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AMENDED MEMORANDUM OF DECISION

Re: Defendant Celltech's Motion for Judgment on the Pleadings and Defendant Genentech's Motion for Summary Judgment

On September 30, 2003, Plaintiff Celltech R&D Ltd. ("Celltech") filed a Motion for Judgment on the Pleadings. On October 31, 2003, Genentech, Inc. ("Genentech") filed a Motion for Summary Judgment on Plaintiffs' Antitrust Claims. The Court heard oral argument on December 15, 2003 and took these matters under submission.

## BACKGROUND

### I. SUMMARY OF THE DISPUTE

This dispute deals with patents claiming a method of producing monoclonal antibodies utilizing recombinant DNA technology. Plaintiff MedImmune is a biotechnology company whose most successful product is Synagis, a drug used to prevent respiratory syncytial virus in children. The Defendants are two biotechnology companies, Celltech and Genentech, and a nonprofit organization, City of Hope. MedImmune's Synagis product utilizes the monoclonal

antibody production techniques covered by the patents at issue. The patent for this technology was originally owned by Celltech, but following the resolution of a priority dispute the technology is now claimed by a patent that has been assigned to Genentech and City of Hope.[1]

MedImmune alleges that Celltech and Genentech illegally resolved the priority dispute between them in a manner that required neither Celltech nor Genentech to give up anything, but that was designed to cause a real loss to others in the industry. Celltech had a patent on the technology at issue that was due to expire in 2006. (Am. Comp. ¶ 13). As part of their settlement, Celltech ceded priority to Genentech. (*Id.* ¶ 12). Genentech then obtained a patent over essentially the same technology; that patent is due to expire in 2018. (*Id.* ¶ 17, ¶ 123). MedImmune claims that this agreement had the effect of creating a 29-year patent monopoly over this technology. (*Id.* ¶ 13).

## II. UNDISPUTED FACTS

The essential facts are uncontroverted. *See* Plaintiff MedImmune, Inc's Statement of Genuine Issues of Material Fact and Responses to Proposed Conclusions of Law in Opposition to Genentech, Inc.'s Motion for Summary Judgment (filed under seal November 17, 2003).

### A. Cabilly and Boss Patents

On April 8, 1983 Genentech filed a U.S. patent application; this patent issued on March 28, 1989 as U.S. Patent No. 4,816,567 with Shmuel Cabilly as the first inventor (the "Cabilly" patent). On November 14, 1984, Celltech filed an application that issued as U.S. Patent No. 4,816,397 on March 28, 1989 with Michael A. Boss as the first inventor (the

[1] References to "Genentech" in the remainder of this memorandum refer to both Genentech and City of Hope.

"Boss" patent). Genentech had a continuation application pending that claimed the benefit of its original April 8, 1983 application date (the "New Cabilly application"). This New Cabilly application was amended to restate the claims of the Boss patent.

B. Interference

Genentech advised the United States Patent and Trademark Office (PTO) of the conflict between the Boss patent and Genentech's pending New Cabilly application. On February 28, 1991, the PTO's Board of Patent Appeals and Interferences ("Board") declared Patent Interference No.102,572 between the Boss patent and Genentech's pending continuation application. On August 13, 1998, the Board awarded priority to Celltech. *Cabilly v. Boss*, 55 U.S.P.Q.2d 1238 (Bd. Pat. App. & Interf. 1998).

C. § 146 Action

On October 9, 1998, Genentech commenced an action under 35 U.S.C. §146 ("the § 146 action") to overturn the Board's priority determination. During the § 146 action, Genentech produced a draft patent application that had not been produced during the interference proceeding before the PTO.

Genentech filed a summary judgment motion in the § 146 action. On July 28, 2000 the Honorable Maxine M. Chesney, United States District Judge for the Northern District of California, heard argument on Genentech's motion for summary adjudication. Judge Chesney denied Genentech's summary judgment motion on the ground that a triable issue of fact existed.

D. Settlement of the § 146 Action

On the day of the summary judgment hearing, Judge Chesney stated that the parties should consider alternative

dispute resolution or private mediation. Genentech and Celltech engaged in mediation conducted by a retired judge in an effort to resolve the § 146 proceeding. Genentech and Celltech entered into the "Settlement Agreement between Genentech, Inc. and Celltech Chiroscience Limited" ("Settlement Agreement") on March 2, 2001. On the same day, Genentech and Celltech also entered into the "Amended and Restated License Agreement between Genentech, Inc. and Celltech Chiroscience Limited" ("ARLA").

On March 6, 2001, Genentech and Celltech filed a Notice of Settlement and Joint Request for Entry of Settlement Instruments, a Proposed Order Regarding Resolution of Interference ("Proposed Order"), and a Proposed Judgment. On March 14, 2001, Celltech and Genentech participated in a telephonic status conference before Judge Chesney. Revised versions of the Proposed Order and Proposed Judgment were subsequently submitted by Celltech and Genentech. The Order and Judgment were executed by Judge Chesney on March 16, 2001.

E. Obtaining the '415 Patent

On June 1, 2001, Genentech filed certified copies of the District Court's Judgment with the PTO Board. *Cabilly v. Boss*, 60 U.S.P.Q.2d 1752, 1755 (Bd. Pat. App. & Interf. 2001). The PTO Board directed Genentech's application to be returned to an Examiner.

On September 13, 2001 Genentech, through its lawyer and its patent agent, submitted documents relating to Genentech's pending application to the PTO and participated in an interview with representatives of the PTO on the same subject. Subsequently, Genentech submitted a Supplemental Information Disclosure statement to the PTO and, on October 4, 2001, participated in an additional interview with representatives of the PTO.

On December 18, 2001, the PTO issued Genentech's pending continuation application as United States Patent No. 6,331,415B1 (the the "New Cabilly" patent).

F. MedImmune Files Suit

MedImmune filed its initial Complaint in this case on April 11, 2003. On August 13, 2003, Plaintiff MedImmune, Inc. served its First Amended Complaint ("Am. Comp."); its Initial Disclosures were served on August 21, 2003.

## LEGAL STANDARD

Although Celltech's and Genentech's motions both rely on the *Noerr-Pennington* doctrine, Celltech's motion is based on Rule 12(c) of the Federal Rules of Civil Procedure (FRCP), whereas Genentech's is a summary judgment motion made under FRCP Rule 56(c). This Court has considered the same evidence in consideration of each motion, thus both motions will be treated as motions for summary judgment. Rule 12(c) explicitly permits this: "If, on a motion for judgment on the pleadings, matters outside the pleadings are presented to and not excluded by the court, the motion shall be treated as one for summary judgment . . .". FRCP, Rule 12(c); *see Hal Roach Studios*, 896 F.2d 1542, 1550 (9th Cir. 1989) ("judgment on the pleadings is improper when the district court goes beyond the pleading to resolve an issue; such a proceeding must properly be treated as a motion for summary judgment").

Summary judgment is appropriate when the submissions show that "there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as matter of law." FRCP Rule 56(c); *Celotex Corp. v. Catrett*, 477 U.S. 317, 322-26 (1986). For the purposes of this motion, MedImmune is entitled to all reasonable inferences that may be drawn from the evidence it cites. *Eisenberg v. Ins. Co. of N. Am.*, 815 F.2d 1285, 1289 (9th Cir. 1987) ("[T]he non-

moving party's evidence is to be taken as true and all inferences are to be drawn in the light most favorable to the non-moving party."). Furthermore, if MedImmune adduces direct evidence of a genuine issue of fact, such evidence may not be weighed against the Defendants' evidence but must be submitted to the trier of fact for resolution. *Id.*

## ANALYSIS

The Defendants ask this Court to find that the *Noerr-Pennington* doctrine bars MedImmune from pursuing its federal antitrust claims (Counts 5 and 6 of the Amended Complaint), state law antitrust claims (Counts 8 and 9), and the state unfair competition claim (Count 10).

The parties agree that California law follows *Noerr-Pennington*, and thus that a decision as to the *Noerr-Pennington* issues will resolve the question of immunity to MedImmune's Cartwright Act and unfair competition claims as well as the Sherman Act claims. Consequently, this discussion focuses on whether the *Noerr-Pennington* doctrine applies to the facts of this case as pled or otherwise established.

### I. The *Noerr Pennington* Doctrine

#### A. State Action Immunity: The Basis for *Noerr-Pennington*

The *Noerr-Pennington* doctrine essentially grants antitrust immunity to parties engaged in petitioning activities. This doctrine has its basis in the state action immunity doctrine—the idea that the government cannot be held liable for anticompetitive acts because the Sherman Act prohibits only those anticompetitive conditions that are sought to be or are created by "individuals or combinations of individuals or corporations." *Standard Oil Co. v. United States*, 221 U.S. 1, 51-62 (1911). States cannot be held liable under the Sherman Act because "nothing in the language of the Sherman Act or in its history suggests that its purpose was to restrain a state

or its officers or agents from activities directed by its legislature." *Parker v. Brown*, 317 U.S. 341, 351 (1942).

B. Antitrust Immunity for Petitioning Activities

The corollary to the state action immunity doctrine is the idea that the conduct of private individuals petitioning the government for anticompetitive action can not be restricted by the antitrust laws, an idea that is known as the *Noerr-Pennington* doctrine.

*1. Establishing Petitioning Immunity*

The competition between railroads and the trucking Industry over long-distance transportation of freight gave the Supreme Court its first opportunity to consider whether antitrust liability could result from attempting to influence the government to pass anticompetitive laws. *Eastern R.R. Presidents Conference v. Noerr Motor Freight, Inc.*, 365 U.S. 127 (1961). In *Noerr* the trucking industry sought relief under the antitrust laws when a consortium of railroad executives conducted a campaign to sully the image of the trucking industry and obtain the passage of laws restricting freight trucking. 365 U.S. at 129-32. The *Noerr* Court recognized that "no violation of the Act can be predicated upon mere attempts to influence the passage or enforcement of laws" and ruled that the railroads could not be held liable for the effects of their campaign. *Id.* at 141-43. The Court held that the Sherman Act does not prohibit two or more persons from associating together in an attempt to persuade the legislature or the executive to take particular action with respect to a law that would produce a restraint or a monopoly"). *Id.* at 136.

Although *Noerr* dealt only with petitioning lawmakers, later cases made it clear that petitioning the executive and judicial branches was protected as well: "the right to petition extends to all departments of the Government." *California Motor Transport Co. et al. v. Trucking Unlimited et al.*, 404 U.S. 508, 510 (1972) (applying *Noerr* immunity to peti-

tioning the courts);[2] *United Mine Workers of America v. Pennington et al.*, 381 U.S. 657, 671 (1965) (applying *Noerr* immunity to petitioning an executive official).[3]

*2. Justification for Petitioning Immunity*

The Noerr Court stated two reasons for concluding that Congress did not intend petitioning activities to be regulated by the Sherman Act.

First, the Court noted that "the whole concept of representation depends on the ability of the people to make their wishes known to their representatives." *Noerr*, 365 U.S. at 137. The imposition of antitrust liability for attempts to influence government could chill those communications and would thus be detrimental to democratic government. *Id.* To hold that people cannot freely inform their representatives of their wishes would impute to Congress an attempt to regulate political activity, a purpose that the Court found unsupported by the legislative history of the Sherman Act. *Id.*

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[2] In *California Motor Transport*, a group of highway carriers attempted to resist and defeat a competitor group's applications for operating rights by seeking reviews and appeals of agency and court decisions on the applications. 404 U.S. at 509. The Court found that "the right of access to the courts is indeed but one aspect of the right of petition" and thus that "it would be destructive of rights of association and of petition to hold that groups with common interests may not, without violating the antitrust laws, use the channels and procedures of state and federal agencies and courts to advocate their causes and points of view respecting resolution of their business and economic interests *vis-a-vis* their competitors." *Id.* at 510-11.

[3] In *Pennington*, the Court considered the legality of a joint effort by a coal workers union and large companies in the industry to obtain establishment from the Secretary of Labor of a minimum wage that would drive smaller companies out of the industry. *United Mine Workers of America v. Pennington et al.*, 381 U.S. 657, 660 (1965). The Court found that *Noerr* made it clear that the union and large companies could not be held liable for any injuries the plaintiff suffered from the action of the Secretary of Labor. *Id.* at 671.

Second, the Court recognized that the First Amendment's right of petition could be violated by imposing antitrust liability on petitioning activities. *Id.* at 138. The Court found that it could not "lightly impute to Congress an intent to invade these freedoms." *Id.*

C. Petitioning for the New Cabilly Patent

The *Noerr-Pennington* doctrine confers immunity where petitioners "attempt to persuade [the government] to take particular action with respect to a law that would produce a restraint or monopoly." *Noerr* 365 U.S. at 136. In this case, the "particular action(s)" that the Defendants sought that would "produce a restraint or monopoly" were the resolution of priority and the issuance of the New Cabilly patent.

As MedImmune suggested in oral argument, there were two basic steps necessary to the issuance of the New Cabilly patent: 1) establishing priority and 2) resolving the other patent issues before the PTO. As is discussed below, this Court finds that petitioning was involved in each of these two steps.[4] Consequently, this Court finds that the *Noerr-*

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[4] Had petitioning been involved in only one of these two steps, immunity would still have been conferred. In prior cases applying the *Noerr-Pennington* doctrine, including *Noerr* itself, only one petitioning activity has been involved. Had only one of the two "prongs" involved petitioning, immunity would still preclude MedImmune's antitrust claims because either through resolving priority or resolving other patent issues, petitioning would still have been involved in obtaining the New Cabilly patent. Immunity protects not only the petitioning activity, but other related activity as well:

> The *Noerr* Court also rejected the proposition that petitioning immunity was limited to injuries flowing directly from governmental action. It held that the railroads were also shielded from liability for the harm the truckers suffered in their relationships with their customers. In the Court's view, that injury was 'incidental' to the defendants' campaign to influence legislation. To impose liabil-

*Pennington* doctrine protects the Defendants from antitrust liability. Summary judgment on the antitrust and related state causes of action is therefore GRANTED in favor of the Defendants.

## II. PRIORITY

In August of 1998 the PTO's Board awarded priority to Celltech. *Cabilly v. Boss*, 55 U.S.P.Q. 1238 (Bd. Pat. App. & Interf. 1998). Overturning this priority decision was a necessary step to obtaining the New Cabilly patent.

### A. MedImmune's Proposed Course of Action

MedImmune contends that priority could have been resolved without government action and that *Noerr-Pennington* immunity does not attach simply because the Defendants chose to resolve priority through Judge Chesney's Court. According to MedImmune, Celltech needed only to file a disclaimer under 35 U.S.C. § 253 to cancel the claims of the Boss patent. Then, according to MedImmune, the PTO would have automatically issued the New Cabilly patent. This argument is both inconsequential and inaccurate.

#### *1. The Availability of Non-governmental Alternatives*

MedImmune has failed to cite, and this Court has been unable to find, any law to support the proposition that immunity is unavailable if the anti-competitive result *could* have occurred without government action, even though the result does not actually occur that way. "[W]here a restraint upon trade or monopolization is the result of a valid

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ity for such incidental effects would 'be tantamount to outlawing' the petitioning activity itself.

*Sessions Tank Liners, Inc. v. Joor Manufacturing, Inc.*, 17 F.3d 295, 299 (9th Cir. 1994). Even if only one "prong" were held to be protected petitioning activity, the Defendants' involvement in the other "prong" would likely be incidental activity as described in *Joor*.

governmental action, as opposed to private action, those urging the governmental action enjoy absolute immunity from antitrust liability for the anti-competitive restrain." *Joor*, 17 F.3d at 301 (quoting *Allied Tube & Conduit Corp. v. Indian Head, Inc.*, 486 U.S. 492, 498 (1988), and *Noerr*, 365 U.S. at 136). The antitrust immunity that the government enjoys, and that petitioners who urge government action correspondingly enjoy, is not dependent on their being a non-governmental way to have achieved the anti-competitive result; it depends simply on whether the alleged violation actually involved petitioning.

*2. MedImmune's Proposed Alternative*

It is simply not true that the New Cabilly patent would have issued in any ministerial way had Celltech utilized § 253 to cancel the claims of the Boss patent. Even if Celltech had cancelled its claims, the Board's outstanding priority decision would still have needed to be overturned.[5]

MedImmune argues that had Celltech cancelled the claims of the Boss patent, the patent would have been treated as never having existed. MedImmune claims that PTO procedure would then have provided for an entry of judgment against Celltech. It is true that when a party involved in an interference claims under § 253 such that all claims corresponding to the count(s) at issue in the interference are deleted, the Board *may* enter judgment against the party. 37

[5] As is discussed further in Part II, even if MedImmune's argument were correct and priority could have been resolved without government action, petitioning was still a necessary part of the application for the New Cabilly patent. As is illustrated by the PTO's refusal to obey Judge Chesney's order and issue the New Cabilly patent once Judge Chesney had declared Genentech the winner of the priority dispute, the PTO does not act ministerially in issuing patents, even when priority has been resolved. *Cabilly v. Boss*, 60 U.S.P.Q. 1752, 1756 (Bd. Pat. App. & Interf. 2001).

CFR § 1.662. However, this is still a matter of discretion, and nothing in the regulations suggests that it is done in a ministerial or automatic way.[6]

No law supports MedImmune's contention that *Noerr-Pennington* immunity does not attach to petitioning if the petitioner's desired result could have been accomplished through means not involving petitioning. Even if this proposition had support in the law, it would not help MedImmune in this case because there was simply no non-petitioning means for priority to be resolved, or for the PTO to evaluate other patent issues. The process leading up to the New Cabilly patent necessarily involved petitioning.

As petitioning would have had to have occurred for the New Cabilly patent to issue even if the Defendants had followed the route MedImmune proposed, and as no law suggests that whether non-petitioning alternatives are available is even relevant, the more important question is whether the petitioning actually involved in resolving priority confers *Noerr-Pennington* immunity.

B. Judge Chesney's Order

The route that the Defendants actually chose to resolve priority involved petitioning. MedImmune argues that merely asking a Judge to approve settlement is not petitioning sufficient to confer immunity, but even if they are right on this point of law, those facts are not what occurred in this

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[6] That § 1.662 is not ministerial provides further support for the idea that an inquiry into whether non-governmental alternatives are available is meaningless. Even if the § 253 procedure had been employed, there is no guarantee that this would have resolved priority. This Court cannot fault the parties for proceeding in a manner that had more certainty—petitioning Judge Chesney for an Order that the Board was willing to accept as determinative as to priority. *See Cabilly v. Boss*, 60 U.S.P.Q.2d 1752, 1757 (2001).

case. MedImmune further argues that even if approval of a settlement does confer immunity, the availability of immunity depends in some way on the process involved in the approval. That is simply not true. Finally and most importantly, MedImmune contends that misrepresentations to Judge Chesney nullify any immunity that might otherwise have attached. This Court finds that no misrepresentations have been pled that would allow this Court to conclude that the Defendants have lost their right to *Noerr-Pennington* immunity.

*1. Approving a Settlement Agreement*

The parties seem to agree that a court's stamp of approval will not immunize private anti-competitive agreements; genuine petitioning is necessary for *Noerr-Pennington* immunity to apply. Genentech concedes that settlements that merely require compulsory filings, ministerial agency actions, or inconsequential court orders such as Rule 41(a) dismissals do not raise a *Noerr-Pennington* defense.

This case can be distinguished from those that do not raise *Noerr-Pennington* questions because this is not a case of the government acting in some way on an agreement that is independently anti-competitive, but the very anti-competitiveness of the agreement depends on the government exercising its discretion to create an anti-competitive result. MedImmune attempts to characterize the settlement agreement itself as anti-competitive, and argues that Judge Chesney's role in approving the settlement cannot immunize it. This is a mischaracterization of the legal effect of the agreement and the role of the government in creating the alleged antitrust violations of which MedImmune complains. This is not a case of an anticompetitive private agreement receiving immunity because it passed through government hands in some ministerial way. Here, the very anti-competitiveness of the agreement depended on the government

exercising its independent power to decide priority and issue the New Cabilly patent.[7]

The Defendants in this case did not merely present their settlement to Judge Chesney for approval; they sought a Judgment and an Order as well. The documents that she signed accomplished results, such as overturning the Board's priority decision, that could not have been accomplished through private agreement. It was these documents—the results of the Defendants' petitioning and Judge Chesney's order—that resolved the issue of priority.

*2. Judge Chesney's Process*

It does not matter whether Judge Chesney ever reached a "considered, substantive judgment," (to use MedImmune's phrase), that Genentech deserved priority. To evaluate this question would require deconstructing the decision-making process, which is exactly what the Ninth Circuit forbade in *Joor*. 17 F.3d at 300. Whether the decisionmaker involved made a "considered, substantive" judgment has not been evaluated in prior cases applying *Noerr*, and this Court declines to add that requirement to the *Noerr-Pennington* doctrine. It does not matter how or why Judge Chesney reached her decision. It matters only that she had the discretion to resolve priority in favor of Genentech and she did so.

*3. Alleged Misrepresentation*

MedImmune's most compelling attempt to avoid *Noerr-Pennington* immunity is its claim that misrepresentations to the Court preclude Noerr immunity. Where misrepresentations to a court "deprive the litigation of its legitimacy" they

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[7] MedImmune makes one antitrust arguement that does not depend on the issuance of the New Cabilly patent. This argument—that Genentech and Celltech engaged in illegal price fixing—is addressed in Part III of this Analysis.

can cause a party to lose *Noerr-Pennington* immunity. *Kottle v. Northwest Kidney Centers*, 146 F.3d 1056, 1060 (9th Cir. 1998) (noting that misrepresentations to the court may cause litigation to be deemed a sham, and thus fall within an exception to *Noerr-Pennington* immunity). MedImmune alleges three misrepresentations to the Court.

First, MedImmune claims that the Defendant's statement to the Court that Genentech's New Cabilly Patent had priority over the Boss patent was a misrepresentation. This was, however, the key issue in the litigation—any settlement agreement had to make a representation one way or the other on this issue and that representation was sure to be contradictory to a position that one of the parties had taken earlier in the litigation. *Kottle* indicates that disputed issues from the underlying litigation cannot be recast as misrepresentations. 146 F.3d at 1063.

Second, MedImmune asserts that the Defendants' statement that the New Cabilly patent did not have defects that should bar its issuance was a misrepresentation. It is not clear from the facts that this statement was a misrepresentation—the fact that the PTO issued the New Cabilly patent suggests that it was at least not a gross misrepresentation. Even if MedImmune could establish that this was a misrepresentation, it would not change the result. The PTO did not rely on Judge Chesney's determination that the New Cabilly patent should issue, thus MedImmune could not have sustained injury from this order. The Defendants consequently have no reason to claim immunity for petitioning for this order, and there is therefore no consequence to a determination that a misrepresentation precipitated the order.

Third, MedImmune alleges that the Defendants misrepresented the law by suggesting to Judge Chesney that Genentech should be granted priority if it demonstrated conception. As students learn in the first days of any patent law class, priority is awarded to the first to reduce to practice, unless the

first to conceive works diligently to reduce the idea to practice. This Court must assume that Judge Chesney was not misled by any statement to the contrary. *Walton v. Arizona*, 497 U.S. 639, 653 (1990)("Trial judges are presumed to know the law and to apply it in making their decisions"), cited in *Beaty v. Stewart*, 303 F.3d 975, 986.(9th Cir. 2002).

## II. PTO PROSECUTION

The parties agree that attempts to obtain the issuance of a patent from the PTO are ordinarily covered by *Noerr-Pennington*. However, a patentee may be subject to antitrust liability for enforcing a patent obtained through knowing and willful fraud on the patent office. *Walker Process Equip. v. Food Mach. & Chem. Corp.*, 382 U.S. 172, 177 (1965); *Nobelpharma AB, et al. v. Implant Innovations, Inc.*, 141 F.3d 1059, 1068 (discussing *Walker Process* fraud and the sham exception to *Noerr-Pennington* as two ways a patentee could be found liable in antitrust).[8] MedImmune argues that in this case the Defendants committed fraud on the patent office that prevents *Noerr-Pennington* immunity from attaching. This argument fails because in its Amended Complaint, MedImmune does not plead fraud.

MedImmune's *Walker Process* theory is not supported in the pleadings. Although MedImmune argues that it "asserts with reference to specific facts, at least forty times, that Genentech's omissions and misrepresentations were intentionally made with deceptive intent," Opposition at 18, a review of the Amended Complaint reveals that it is inequitable conduct, not fraud, that appears in the pleadings. Fraud

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[8] Neither party has alleged that the sham exception to the *Noerr-Pennington* doctrine applies in this case. MedImmune does allege that the Defendants made misrepresentations to Judge Chesney, and misrepresentations can make litigation into a sham, *Kottle*, 146 F.3d at 1060, but Part I(C) of this Analysis explains that misrepresentations have not be adequately alleged.

(as that term is meant in *Walker Process*) and inequitable conduct are different legal concepts, and it is simply not the case that inequitable conduct pleadings can be read as affirmatively pleading fraud for all purposes. MedImmune has not pled facts sufficient to support *Walker Process* fraud.

A. Distinguishing Inequitable Conduct from Fraud

There is a significant difference between *Walker Process* fraud and inequitable conduct, a state of law that was highlighted to this Court by Plaintiff earlier in this litigation.[9] The Federal Circuit discussed this distinction in *Nobelpharma*, where it noted that "inequitable conduct is a broader, more inclusive concept than the common law fraud needed to support a *Walker Process* counterclaim," and that "[i]nequitable conduct in fact is a lesser offense than common law fraud, and includes types of conduct less serious that "knowing and willful" fraud. 141 F.3d at 1069; *see* also *Norton v. Curtiss*, 433 F.2d 779, 793 (C.C.P.A. 1970) (contrasting inequitable conduct with conduct "sufficiently reprehensible so as to carry with it the consequences of technical fraud").

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[9] When filing its Amended Complaint, MedImmune assured this Court that it was making changes to its inequitable conduct claim to "make it consistent with the Court's Order dated August 11, 2003." The August 11, 2003 Order to which MedImmune refers granted Genentech's Motion to Dismiss an inequitable conduct claim but allowed MedImmune leave to amend it. In defending against this Motion to Dismiss, MedImmune argued that the heightened pleading standard of FRCP Rule 9(b) applied only to fraud claims. MedImmune took pains to distinguish its inequitable conduct claim from a fraud claims. *See* Plaintiff MedImmune, Inc's Opposition to Motion by Defendant Genentech, Inc. to Dismiss the Third and Eleventh Causes of Action (filed July 14, 2003) at 9. It now appears that MedImmune is trying to argue that in amending its inequitable conduct claim, it converted it into a fraud claim. This argument is both disingenuous and, as is discussed in more detail above, not supported by the pleadings.

The *Nobelpharma* court contrasted the nature of the claims and the remedies available for fraud, as that term is meant in *Walker Process* with the claims and remedies for inequitable conduct. The court noted that inequitable conduct is an equitable defense, whereas fraud is an affirmative claim. 141 F.3d at 1070. It also compared the treble damages available in antitrust with the remedies of patent unenforcability and possibly attorney's fees that are available for inequitable conduct. *Id.*

B. Pleading Fraud

MedImmune alleges that Genentech acted fraudulently by 1) failing to alert the PTO to the enablement problems relating to the refolding aspect of the claimed invention, 2) failing to disclose its prior inconsistent position with respect to a material prior art reference known as the Vallé reference, 3) failing to disclose certain anticipatory prior art about which it allegedly knew and 4) burying anticipatory prior art in the voluminous documents that composed its submission. Even if this Court were willing to look past the disingenuousness of MedImmune's assertation that what the parties-and this court were told was an inequitable conduct claim has morphed into a fraud claim, MedImmune's pleadings do not allege facts that, if proved, would allow this Court to conclude that the elements of *Walker Process* fraud had been satisfied.

In *Norton*, the court that preceded the Federal Circuit explained the elements of what the *Nobelpharma* court called "'fraud' as that term was used by the Supreme Court in *Walker Process*," 141 F.3d at 1069:

> traditionally, the concept of "fraud" has most often been used by the courts, in general, to refer to a type of conduct so reprehensible that it could alone form the basis of an actionable wrong (e.g., the common law action for deceit.) That narrow range of conduct, now frequently referred to as 'technical' or 'affirmative'

> fraud, is looked upon by the law as quite serious. Because severe penalties are usually meted out to the party found guilty of such conduct, technical fraud is generally held not to exist unless the following indispensable elements are found to be present: 1) a representation of a material fact, 2) the falsity of that representation, 3) the intent to deceive or, at least, a state of mind so reckless as to the consequences that it is held to be the equivalent of intent (scienter), 4) a justifiable reliance upon the misrepresentation by the party deceived which induces him to act thereon, and 5) injury to the party deceived as a result of his reliance on the misrepresentation.

*Norton*, 433 F.2d at 792-93, cited in *Nobelpharma*, 141 F.3d at 1069-70.

To fulfill the requirements of *Walker Process*, "a misrepresentation or omission must evidence a clear intent to deceive the examiner and thereby cause the PTO to grant an invalid patent." *Nobelpharma*, 141 F.3d at 1070. This standard is a difficult one to meet, as the *Nobelpharma* court explains:

> A finding of *Walker Process* fraud requires higher threshold showings of both intent and materiality than does a finding of inequitable conduct. Moreover, unlike a finding of inequitable conduct, . . . a finding of *Walker Process* fraud may not be based upon an equitable balancing of lesser degrees of materiality and intent. Rather, it must be based on independent and clear evidence of deceptive intent together with a clear showing of reliance, i.e. that the patent would not have issued but for the misrepresentation or omission.

141 F.3d at 1070-71 (internal citations omitted). MedImmune's pleadings fail to fulfill the requirements of *Walker Process* fraud, because they suggest neither "independent or

clear evidence of deceptive intent" nor that "the patent would not have issued but for the misrepresentation or omission" (i.e. reliance).

In fact, the PTO is presumed to be aware of the references before it, which would include the court documents discussing enablement problems, the Vallé reference, and the other prior art that was submitted, even if it was buried. *See American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350, 1359 (Fed. Cir. 1984) (noting that a PTO examiner is presumed to have considered the documents submitted). Even inequitable conduct cannot be found on the basis of a reference that was cited to the examiner. *Fiskars, Inc. v. Hunt Manufacturing Co.*, 221 F.3d 1318, 1327 (Fed. Cir. 2000)("An applicant cannot be guilty of inequitable conduct if the reference was cited to the examiner, whether or not it was a ground of rejection by the examiner").

As for references that were not before the PTO, omissions cannot be fraudulent absent evidence of fraudulent intent. *Nobelpharma* states: "for an omission such as failure to cite a piece of prior art to support a finding of *Walker Process* fraud, the withholding of the reference must show evidence of fraudulent intent. A mere failure to cite a reference to the PTO will not suffice." 141 F.3d at 1071. MedImmune does not plead facts that would support a finding of fraudulent intent.

MedImmune cannot show that the PTO relied on alleged misrepresentations about references that were before it because the examiner is presumed to have independently considered the references, and MedImmune cannot base a *Walker Process* claim on the omission of references without alleging independent evidence of deceptive intent. Thus even if each of the allegations of MedImmune's Amended Complaint were true, they would be insufficient to support a claim of *Walker Process* fraud.

## III. PRICE FIXING

MedImmune has one antitrust argument that does not implicate *Noerr-Pennington* considerations. This argument is based on the ARLA between Celltech and Genentech, and essentially claims that the ARLA was an illegal price fixing agreement. The ARLA provides that Celltech will receive royalty payments from Genentech that are to be paid from the royalties that Genentech obtains from third parties, including MedImmune. Because the ARLA provides that Genentech will "use best efforts" to charge these third parties at least certain minimum royalties, MedImmune asserts that the ARLA is a price-fixing agreement.

There are at least two problems with MedImmune's theory: 1) price-fixing is not pled in the Amended Complaint and 2) MedImmune would not have standing to make this price-fixing claim even if it were in the Amended Complaint.[10]

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[10] In addition to these two preliminary problems, this Court's review of the ARLA leads to the conclusion that price-fixing is not a part of the agreement. Section 3.02 of the agreement lists "Royalties Payable by Genentech for Third Party Products." The first five subparts of §3.02 list specific products for which Celltech was receiving royalties under the Boss patent, and specifies the royalty rate that Genentech would pass-through for sales of that product once Genentech owned the patent to the technology. ARLA §3.02(a)-(e), Winters Declaration, Ex. 14, pp. 11-14 (filed under seal October 31, 2002).

The paragraph about which MedImmune complains provides:

> Genentech shall be obligated to pay Celltech the royalties specified in paragraphs 3.02(a)-(e) on Net Sales by a third party licensee or sublicensee of a particular Antibody product only if the amount of payments received by Genentech in a Calendar Quarter from its third party licensee or sublicensee for such product, after deduction of the portion thereof that Genentech is obligated to pay to the City of Hope, equals or exceeds the royalty owed to Celltech in such Calendar Quarter for such Net Sales. Genentech shall, and Genentech shall require that its Affiliates shall, i) use best efforts to impose upon all third parties which are the licensees and sublicensees

MedImmune's price-fixing theory does not appear in the Amended Complaint. The Amended Complaint does state that the settlement is "illegal and anticompetitive" under either the per se or rule of reason theory. Am. Comp. ¶¶ 9, 170-72. It does not, however, allege price fixing in any less general way. MedImmune has not alleged facts in its Amended Complaint that would, if true, suggest that the settlement involved price fixing.

Even if MedImmune had alleged price-fixing in the Complaint, it is difficult to see how the paragraph about which MedImmune complains (*see* n.8) affects MedImmune. The only MedImmune product affected the §3.02 of the ARLA is Synagis, and the parties agree that MedImmune signed a license agreement with Genentech regarding Synagis prior to entering the settlement agreement or the ARLA. As MedImmune's royalties for Synagis are established by this licensing agreement, MedImmune would be unaffected by any price-fixing in the ARLA even if it were adequately alleged. MedImmune claims to be worried about its other "pipeline products" but the plain language of the ARLA and Genen-

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with respect to the Antibody products referred to in paragraphs 3.02(a)-(e) an obligation to pay to Genentech (or the relevant Affiliate) an amount at least sufficient to meet the royalty obligations set out in paragraphs 3.02(a)-(e), and ii) use reasonable and diligent efforts in good faith to collect such amounts from such third parties.

ARLA §3.02(f), Winters Dec. Ex. 14 pp.14. The paragraph continues on to make provisions that would take effect if Genentech did not collect from third parties royalties in the amounts promised to Genentech. This include passing-through the lesser royalty amount and accruing the remainder for payment at a later time. *Id.* at pp. 14-15. This paragraph requires Genentech to attempt to maintain at least the royalty rates that Celltech was receiving so that Celltech receives the consideration it is expecting from ceding priority, but it does not set a minimum royalty rate at which a license to the Cabilly Patent will be set. Although this Court declines to decide the price fixing issue because of the pleading and standing problems discussed in the text, it is unlikely that such a claim would be successful.

tech's representations in oral argument make it clear that § 3.02 of the ARLA does not cover any MedImmune product, current or future, other than Synagis.

MedImmune has not pled price-fixing, and has no standing to plead that § 3.02 of the ARLA constitutes price-fixing. Consequently, MedImmune can not establish a antitrust claim based on price-fixing.

## CONCLUSION

Where a plaintiff "fail[s] to prove that its injuries result from anything other than governmental action," *Noerr-Pennington* immunity will attach. *Joor*, 17 F.3d at 296. With the exception of the price fixing argument dismissed in Part 3 above, MedImmune has not pled an injury that was the result of the Defendants' settlement agreement. In the absence of government action in resolving priority and issuing the New Cabilly patent, MedImmune would have suffered no harm from the Defendants' settlement. Because the alleged "restraint upon trade or monopolization is the result of valid governmental action, as opposed to private action," *Noerr-Pennington* immunity applies. *Joor*, 17 F.2d at 301.

Based upon the fact that *Noerr-Pennington* immunity bars MedImmune's antitrust and related state claims, and in light of MedImmune's failure to adequately plead any antitrust violation (such as price-fixing in the ARLA) that is not barred by *Noerr-Pennington*, summary judgment for the Defendants is hereby GRANTED with respect to the fifth, sixth, seventh, eighth, ninth, and tenth causes of action in the First Amended Complaint.

IT IS SO ORDERED

DATED: January 12, 2004

/s/ Mariana R. Pfaelzer
Honorable Mariana R. Pfaelzer
United States District Judge

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Feb. 18, 2004]

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Case No. CV 03-2567 MRP

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MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

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MEMORANDUM OF DECISION
RE: Celltech's Motion For Entry of Final Judgment

On January 20, 2003, Defendant Celltech R&D Ltd. ("Celltech") filed a Motion for Entry of Final Judgment ("Motion"). Having determined that oral argument will not assist the Court in considering this motion, this Court hereby vacates the hearing scheduled for February 23, 2004, and GRANTS Celltech's motion.

BACKGROUND

I. The Case

A. Basic Facts

This case involves a technique for using recombinant DNA technology to produce monoclonal antibodies. Plaintiff MedImmune's most successful product, Synagis, requires the use of this technology. MedImmune asserts that the technology at issue was patented by Defendant Celltech, but is now covered by a patent that has been assigned to Defendants Genentech and City of Hope. This, according to MedImmune, had the effect of creating an illegal twenty-nine year patent monopoly.

B. Claims

MedImmune's First Amended Complaint asserts ten claims against three named defendants. First Amended Complaint ("FAC") ¶¶ 131-215. The first claim is for declaratory judgment of rights and obligations under MedImmune's license agreement with Genentech. FAC ¶¶ 131-33. Three claims are patent claims (invalidity, unenforceability, and non-infringement). FAC ¶¶ 134-64. The final six claims are state and federal antitrust and unfair competition claims. FAC ¶¶ 165-201.

C. Parties

Plaintiff MedImmune brings claims against three defendants. Genentech, Inc. ("Genentech") is a defendant as to every claim. FAC ¶¶ 131-201. City of Hope is a defendant only as to the patent claims. FAC ¶¶ 134-64 (Second, Third, and Fourth Causes of Action). Celltech, the moving party in this motion, is a defendant as to most of the antitrust and unfair competition claims, but none of the contract or patent claims. *See* FAC ¶¶ 165-180, ¶¶ 186-201 (Fifth, Sixth, Eighth, Ninth, and Tenth Causes of Action).

II. Summary Judgment

This Court recently granted summary judgment against MedImmune on the antitrust and unfair competition causes of action at issue in this case. Memorandum of Decision Re: Defendant Celltech's Motion for Judgment on the Pleadings and Defendant Genentech's Motion for Summary Judgment. ("Summary Judgment Decision") (filed 12/23/03, amended 1/14/04). The antitrust and unfair competition claims against Celltech and Genentech were disposed of by this summary judgment decision. Consequently, there are now no pending causes of action against Celltech.

III. Motion for Entry of Final Judgment

Celltech filed its Motion on January 20, 2003. On February 6, 2004, Genentech joined Celltech's motion. Genentech, Inc.'s Joinder in Celltech's Motion for Entry of Judgment Pursuant to Rule 54(b) ("Genentech Joinder") (filed Feb. 6, 2004). Genentech prefers a single appeal in this case after all issues are resolved and would not have sought a Rule 54(b) judgment absent Celltech's request. Genentech Joinder at 1, 3. However, if Rule 54(b) judgment is entered, Genentech requests that it be entered as to all the antitrust and unfair competition claims, and that Genentech be included as a party in favor of whom final judgment is entered on these claims to avoid the potential for piecemeal appeals. *Id.*

MedImmune consents to Celltech's Motion. MedImmune filed a statement suggesting that this Court decide this Motion after MedImmune's Motion for Leave to Amend has been decided, and indicating that if leave to amend is denied "MedImmune consents to Celltech's 54(b) Motions as it believes that prompt appellate review of these issues is appropriate." Plaintiff MedImmune, Inc.'s Statement in Response to Defendant Celltech R&D Ltd.'s Motion for Entry of Final Judgment (filed Feb. 6, 2004). Thus, with the exception of Genentech's misgivings, this Motion is unopposed.

ANALYSIS

When multiple claims or parties are involved in an action, a district court may enter final judgment as to one or more of the claims or parties prior to the resolution of the entire case. FRCP Rule 54(b). The federal rule states:

> When more than ore claim for relief is presented in an action . . . or when multiple parties are involved, the court may direct the entry of a final judgment as to one or more but fewer than all of the claims or parties only upon an express determination that there is no just

> reason for delay and upon an express direction for the entry of final judgment.

*Id.; see also Sheehan v. Atlanta Int'l Inst. Co.*, 812 F. 2d 465, 468 (9th Cir. 1987) (finding no abuse of discretion in district court's Rule 54(b) judgment when the court expressly found "no just reason for delay").

An entry of final judgment is appropriate where 1) the judgment is final as to one or more claims and 2) the court properly concludes that there is no just reason for delay. *See W.L. Gore & Assoc. Inc. v. Int'l Medical Prosthetics Research Assoc., Inc.*, 975 F. 2d 858, 861-2 (Fed. Cir. 1992).

I. Finality of Judgment

The statutes governing the courts of appeals limit their jurisdiction to final decisions of the district courts. *See* 28 U.S.C. §1291 (governing most courts of appeals); 28 U.S.C. § 1295(a)(1) (governing the Federal Circuit); *Sears, Roebuck & Co. v. Mackey*, 351 U.S. 427, 435 (1956) (noting that Rule 54(b) "does not relax the finality required of each decision, as an individual claim"). Thus, "[t]he requirement of finality is a statutory mandate and not a matter of discretion." *W.L. Gore*, 975 F.2d at 862. Before entering final judgment, this Court must determine that, according to "traditional notions of finality" and guided by Supreme Court precedent, the judgment is final. *W.L. Gore*, 975 F.2d at 862-64.

A judgment is only final if it is "an ultimate disposition of an individual claim entered in the course of a multiple claims action." *Sears*, 351 U.S. at 436. This Court's summary judgment decision is the ultimate disposition of the antitrust and unfair competition claims that MedImmune brought in this action. After considerable research and consideration, this Court concluded that the *Noerr-Pennington* doctrine applied to bar the antitrust and unfair competition claims against the Defendants. Summary Judgment Decision, at 6-23. MedImmune has been unable to frame antitrust or unfair com-

petition claims that do not hinge on the Defendants' petitioning activities, and is thus unable to assert claims that are not barred by *Noerr-Pennington* immunity.[1] Because the determination that those claims are barred by the *Noerr-Pennington* doctrine "ends the litigation on the merits and leaves nothing for the court to do but execute the judgment" as to those claims this Court's decision that the antitrust and unfair competition claims cannot remain in this case is a final one. *Catlin v. United States*, 324 U.S. 229, 233 (1945).

II. Just Reason for Delay

Appropriate factors for consideration in determining whether there are just reasons for delay include "whether the claims under review were separable from the others remaining to be adjudicated and whether the nature of the claims already determined was such that no appellate court would have to decide the same issues more than once even if there were subsequent appeals." *Curtiss-Wright Corp. v. General Electric Corp.*, 446 U.S. 1, 8 (1980).

A. Separateness of the Claims for Relief

In choosing whether to exercise discretion to enter final judgment as to the antitrust and unfair competition claims, this Court must consider the factual relatedness of those claims to the remaining contract, patent unenforceability, invalidity, and non-infringement claims. *See Cold Metal Process Co. v. United Eng'g & Foundry Co.*, 351 U.S. 445, 452 (1956) (the relationship of the adjudicated claims to the unadjudicated claims is one of the factors which the District

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[1] On or about the same day of this Order, this Court will issue an order denying MedImmune's Motion to File a Second Amended Complaint. Memorandum of Decision re Motion to File Second Amended Complaint (filed 02/17/2004). As is indicated by that Memorandum of Decision, MedImmune's attempts to formulate antitrust and unfair competition claims that avoid the consequences of *Noerr-Pennington* and this Court's order were unsuccessful. *Id.*

Court can consider in the exercise of its discretion). The remaining causes of action (1-4) are not substantially related to those that were the subject of the summary judgment order.

The claim that is potentially the most factually related to the claims resolved by the summary judgment order is MedImmune's patent unenforceability claim. FAC ¶¶ 140-61. In this claim, MedImmune contends that Genentech's patent is unenforceable due to Genentech's alleged inequitable conduct before the PTO.[2] Because part of MedImmune's antitrust claim was based on alleged misrepresentations before the PTO, there may be some factual overlap in these claims. However, any overlap is unlikely to be significant, especially to a court of appeals that will be evaluating whether *Noerr-Pennington* creates immunity, not whether the alleged inequitable conduct creates an antitrust violation.

Even where there is some factual overlap, entry of final judgment may be appropriate if other sufficiently important factors are served. *See Curtiss-Wright*, 446 U.S. at 8, n.2; *Intergraph Corp. v. Intel Corp.*, 253 F.3d 695, 699 (Fed. Cir. 2001) ("Even for claims that arise out of the same transaction or occurrence, sound case management may warrant entry of

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[2] Celltech's statement that this Court "has already held that the inequitable conduct allegations are inadequate to overcome *Noerr-Pennington* immunity" is untrue, and makes no sense. It is true that this Court noted that "attempts to obtain the issuance of a patent from the PTO are ordinarily covered by *Noerr-Pennington*," and found that the exception to this rule—*Walker Process* fraud—did not apply. Summary Judgment Order, 18-23. However, this Court's finding that Genentech's petitioning activity before the PTO cannot be the basis of an antitrust or unfair competition claim in no way precludes MedImmune from arguing that Genentech engaged in inequitable conduct that renders the patent unenforceable. If this Court accepted Celltech's interpretation of the Summary Judgment Order, then it would have to import *Walker Process* into unenforceability analysis, allowing unenforceability claims only when the standards for fraud are fulfilled, and thereby eradicating the concept of inequitable conduct.

partial final judgment.") In this case, a party and a significant portion of easily severable claims were eliminated by the summary judgment order. Entry of final judgment on those claims will allow the *Noerr-Pennington* decision to be heard on appeal if MedImmune chooses to pursue one and will streamline and simplify the resolution of the claims that remain with this Court.

B. Risk of Piecemeal Litigation

Another factor in this Court's decision to enter final judgment on the antitrust and unfair competition claims is consideration of "whether an 'appellate court would have to decide the same issues more than once even if there were subsequent appeals.'" *Curtiss-Wright*, 446 U.S. at 8, *cited in Gore* 975 F.2d at 864. This might be a concern if this Court entered final judgment as to Celltech, but not as to Genentech, because MedImmune could appeal the *Noerr-Pennington* decision as to Celltech right away, and then could appeal the same decision as to Genentech once the entire case was resolved. However, Rule 54(b) allows this Court to enter final judgment not only as to parties whose involvement in the litigation has concluded, but as to claims that have been fully litigated. FRCP Rule 54(b).

This Court's judgment as to the *Noerr-Pennington* issues is final, and there is no reason to delay the parties' ability to appeal this decision if they choose to do so. This Court therefore enters final judgment as to both Celltech and Genentech on the antitrust and unfair competition claims. If MedImmune chooses to appeal the *Noerr-Pennington* decision, they will do so with respect to both Celltech and Genentech and thus the court of appeals will only have to evaluate this Court's *Noerr-Pennington* analysis once.

## CONCLUSION

This Court has fully considered and adjudicated the antitrust and unfair competition claims against Celltech and Genentech. As these issues have been eliminated from the case, final judgment is appropriate. *See Cadillac Fairview v. United States*, 41 F.3d 562, 564 n.l (9th Cir. 1994) ("eliminating issues and parties from a case justifies the entry of final judgment on a claim"); *Alcan Aluminum Corp. v. Carlsberg Financial Corp.*, 689 F.2d 815, 817 (9th Cir. 1982) (affirming Rule 54(b) entry of final judgment where all claims against a party have been decided). As there is no reason to delay appeal on those claims, this Court enters final judgment on the fifth, sixth, seventh, eighth, ninth and tenth causes of action.

MedImmune may pursue the remaining claims (determination of contractual obligations, patent unenforceability, patent invalidity and non-infringement) against Genentech (and City of Hope), but Celltech will no longer be involved as a party.

IT IS SO ORDERED

DATED: February 17, 2004

/s/ Mariana R. Pfaelzer
Honorable Mariana R. Pfaelzer
United States District Judge

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Mar. 12, 2004]

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Case No. CV 03-2567 MRP

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MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

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JUDGMENT

THIS CONSTITUTES NOTICE OF ENTRY AS REQUIRED BY FRCP, RULE 77(d)

For reasons detailed in the Memorandum of Decision Re: Celltech's Motion for Entry of Final Judgment that was filed on February 18, 2004, this Court finds that it has fully considered and adjudicated the antitrust and unfair competition claims in this case. As there is no reason to delay appeal on those claims, this Court enters final judgment on the fifth, sixth, seventh, eighth, ninth and tenth causes of action. This Order is a final judgment for purposes of Fed.R. Civ.P. 54(a). It shall be entered pursuant to Fed.R.Civ.P. 58 and 79(a), and served upon the parties.

IT IS SO ORDERED

DATED: February 19, 2004

/s/ Mariana R. Pfaelzer
Honorable Mariana R. Pfaelzer
United States District Judge

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Mar. 17, 2004]

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Case No. CV03-2567 MRP (CTx)
Hon. Mariana R. Pfaelzer

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MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

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NOTICE OF APPEAL

Notice is hereby given that Plaintiff MedImmune, Inc. in the above named case hereby appeals to the United States Court of Appeals for the Federal Circuit from a Judgment, entered on March 15, 2004, dismissing MedImmune Inc.'s Fifth, Sixth, Seventh, Eighth, Ninth, and Tenth causes of action of its First Amended Complaint, (a copy of which is attached at Exhibit A).

Dated: March 17, 2004 DEWEY BALLANTINE LLP

By: /s/ Jeffrey R. Witham
JEFFREY R. WITHAM
Attorneys for Plaintiff
MEDIMMUNE, INC.

[Exhibit omitted in printing]

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

Case No. CV 03-2567 MRP (CTx)

MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC.; CITY OF HOPE; and CELLTECH R&D LTD.,

*Defendant.*

# GENENTECH'S NOTICE OF MOTION AND MOTION TO DISMISS FOR LACK OF SUBJECT MATTER JURISDICTION; MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT

## NOTICE OF MOTION AND MOTION

PLEASE TAKE NOTICE THAT at 10 a.m. on April 19, 2004, or as soon thereafter as the matter can be heard, before the Honorable Mariana R. Pfaelzer, in Courtroon 12 of the United States District Court for the Central District of California, Defendant Genentech, Inc. ("Genentech") will and hereby does move under Federal Rules of Civil Procedure 12(b)(1) and 12(b)(3) for dismissal of all remaining causes of action, specifically: First Cause of Action (Declaratory Judgment on Contractual Rights and Obligatons), Second Cause of Action (Patent Invalidity), Third Casue of Action (Patent Unenforceability), and Fourth Cause of Action (Non-Infringement).

The motion against all remaining causes of action will be based on the grounds that this Court lacks subject matter jurisdiction over each of the claims and MedImmune lacks standing to bring these claims under the Declaratory Judgment Act.

This motion is based on this Notice of Motion and Motion, on the Memorandum of Points and Authorities filed concurrently herewith, on the pleading and papers on file in this action, and on the oral argument at the hearing on the motion. This motion is made following the conference of counsel pursuant to Local Rule 7-3 that took place on March 8, 2004.

Date: March 22, 2004

Respectfully submitted,
LATHAM & WATKINS LLP

By: /s/ Mark A. Flagel
MARK A. FLAGEL
Attorneys for Defendant
Genentech, Inc.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

Case No. CV-03-2567 MRP (CTx)

MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendant.*

# DEFENDANT CITY OF HOPE'S JOINDER IN DEFENDANT GENENTECH, INC.'S MOTION TO DISMISS FOR LACK OF SUBJECT MATTER JURISDICTION

Defendant City of Hope hereby joins defendant Genentech, Inc.'s Motion to Dismiss for Lack of Subject Matter Jurisdiction. The Federal Circuit's decision in Gen-Probe v. Vysis, Inc., ___ F.3d ___, 2004 WL 405737, Case Nos. 02-1617, 02-1618 (Fed. Cir. Mar. 5, 2004) compels the conclusion that plaintiff MedImmune Inc.'s remaining claims must be dismissed for lack of subject matter jurisdiction.

City of Hope respectfully requests that this Court dismiss MedImmune's remaining claims against City of Hope, specifically: MedImmune's Second Cause of Action (seeking a declaration of Patent Invalidity), Third Cause of Action (seeking a declaration of Patent Unenforceability), and Fourth Cause of Action (seeking a declaration of Non-Infringement).

DATED: March 22, 2004

Respectfully submitted,

IRELL & MANELLA LLP
Morgan Chu
David I. Gindler
Joseph M. Lipner
Jason Linder

By: /s/ Jason Linder
JASON LINDER
Attorneys for Defendant
CITY OF HOPE

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Mar. 29, 2005]

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Case No. CV03-2567 MRP (CTx)
Hon. Mariana R. Pfaelzer

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MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

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# DECLARATION OF DAVID M. MOTT IN SUPPORT OF PLAINTIFF MEDIMMUNE, INC.'S OPPOSITION TO GENENTECH, INC.'S MOTION TO DISMISS FOR LACK OF SUBJECT MATTER JURISDICTION FILED UNDER SEAL

I, David M. Mott, hereby declare as follows:

1. I am the Chief Executive Officer of plaintiff MedImmune, Inc. ("MedImmune").

2. MedImmune is a Delaware corporation with its principal place of business in Gaithersburg, Maryland. MedImmune uses biotechnology to develop and produce antibody therapies.

3. MedImmune's most successful product, Synagis®, is used for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus ("RSV") in pediatric patients at high risk for RSV disease.

4. Research indicates that RSV infects approximately two-thirds of all infants during the first year of life and almost

100% of children by age two. It has also been found that RSV infection can be fatal in high-risk pediatric patients.

5. Synagis® was developed by MedImmune scientists during the early 1990's utilizing recombinant DNA technology.

6. Bringing this life-saving drug to market required a sustained effort spanning many years and costing many millions of dollars. After years of research and development, MedImmune conducted extensive clinical trials of Synagis® to prove to the FDA's satisfaction that this novel drug is not only safe, but also demonstrably effective in preventing RSV.

7. MedImmune obtained FDA approval to sell Synagis® in the U.S. in June of 1998. Synagis® was the first monoclonal antibody approved by the FDA to prevent an infectious disease.

8. MedImmune began selling Synagis® commercially in September 1998. Since then, Synagis® has become one of the most successful pediatric drugs ever marketed in the U.S.

9. Sales of Synagis® have accounted for over 80 percent of MedImmune's revenues from sales since 1999, including 82 percent in 1999; 86 percent in 2000; 89 percent in 2001; 85 percent in 2002; and 86 percent in 2003.

10. Synagis® remains MedImmune's most significant product to date and sales of Synagis® remain the driving force behind the company's revenue.

11. In or around December 2001, I was informed that Genentech, which at the time was one of the largest biotechnology companies in the United States, had been issued United States Patent No. 6,331,415 entitled "Methods of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein" (the "Cabilly II Patent").

12. MedImmune had previously entered into a license agreement with Genentech in 1997 (the "1997 License

Agreement") to obtain certain rights to use Genentech's then-issued United States Patent No. 4,816,567 (the "Cabilly I Patent") and any related continuation or divisional applications, including the then pending application that matured into the Cabilly II Patent.

13. Despite the existence of the 1997 License Agreement, MedImmune has never paid Genentech any royalties under the Cabilly I Patent based on sales of Synagis®.

14. In or around January 2002, I was informed that Genentech had sent a letter dated January 7, 2002 demanding by March 1, 2002, payment of royalties for sales of Synagis® based on the Cabilly II Patent.

15. MedImmune considered Genentech's January 7th letter a clear threat to enforce the Cabilly II Patent against MedImmune. Genentech stated that it was writing "to confirm Genentech's expectation that MedImmune will pay royalties on sales of its Synagis® antibody product."

16. MedImmune disagreed with Genentech's position that royalties were due on March 1, 2002 because the Cabilly II Patent was invalid, unenforceable and/or not infringed by MedImmune's Synagis® product. Accordingly, our chief legal officer, Mr. William C. Bertrand, sent Genentech a letter dated February 13, 2002 asking for Genentech's basis for asserting that royalties were due.

17. Genentech did not provide MedImmune a written response by March 1, 2002, the date by which it had demanded that royalties be paid.

18. It was my understanding and belief, based on Genentech's letter and its public statements about the breadth and importance of the Cabilly II Patent, information within the industry, and practical business realities, that Genentech would terminate the 1997 License Agreement and sue MedImmune for patent infringement based on sales of Synagis® if MedImmune did not make the royalty payments as demanded.

19. Despite MedImmune's belief that the Cabilly II Patent was invalid, unenforceable and/or not infringed by MedImmune's Synagis® product, as Chief Executive Officer, I chose not to risk an immediate lawsuit by Genentech that could threaten sales of Synagis®, a life-saving drug, by the potential imposition of a preliminary or permanent injunction that would prevent MedImmune from selling the product.

20. Accordingly, MedImmune decided to pay royalties under protest (which MedImmune did after the March 1, 2002 deadline imposed by Genentech and the 1997 License Agreement) and subsequently challenge in court whether the Cabilly II Patent was valid, enforceable and/or infringed by MedImmune's Synagis® product.

21. After MedImmune made its first royalty payment, Genentech reasserted that the Cabilly II Patent was valid, enforceable and infringed by Synagis® in a letter dated March 24, 2002.

22. Genentech's January 7th and March 24th letters, along with its public statements, confirmed MedImmune's reasonable apprehension and the basic business reality that unless MedImmune continued to pay royalties before it obtains a court judgment that the Cabilly II Patent is invalid, unenforceable and/or not infringed by MedImmune's Synagis® product, Genentech would promptly terminate the 1997 License Agreement and file an infringement action against MedImmune.

23. This course of action, however, has not been without consequence for MedImmune, as it has paid . . . to Genentech on sales of Synagis® since March 4, 2002 on the Cabilly II Patent (a patent which it believes is invalid, unenforceable and/or not infringed by MedImmune's Synagis® product), including . . . paid during the pendency of this litigation.

I declare under penalty of perjury that the following is true and correct.

Dated: Gaithersburg, Maryland
March 29, 2004

/s/ David M. Mott
DAVID M. MOTT

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

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Case No. CV03-2567 MRP (CTx)

---

MEDIMMUNE, INC.,

*Plaintiff,*

v.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

---

Hon. Mariana R. Pfaelzer

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# DECLARATION OF WILLIAM C. BERTRAND IN SUPPORT OF PLAINTIFF MEDIMMUNE, INC.'S OPPOSITION TO GENENTECH'S MOTION TO DISMISS FOR LACK OF SUBJECT MATTER JURISDICTION [FILED UNDER SEAL]

I, William C. Bertrand, hereby declare as follows:

1. I am the Vice President for Legal Affairs, General Counsel and Corporate Compliance Officer of plaintiff MedImmune, Inc. ("MedImmune").

2. I joined MedImmune on or about November 15, 2001.

3. In my capacity at MedImmune, I have responsibility for all legal matters, including all litigation, intellectual property and contractual matters. As part of that responsibility, I am generally familiar with the maintenance of records relating to MedImmune's negotiations with third parties with respect to intellectual property rights.

4. A true and correct copy of a letter from Clint Rogers of Genentech to Michael Richman of MedImmune dated June

11, 1997, enclosing a true and correct copy of an agreement between MedImmune and Genentech executed by MedImmune on or about June 2, 1997 (the "1997 License Agreement"), is attached hereto as Exhibit 1.

5. It is my understanding based on MedImmune's business records that, other than paying the initial $ . . . license grant fee, MedImmune did not make any royalty pay-ments on any sales of its Synagis® product under the 1997 License Agreement during the first four and a half calendar years the license was in effect.

6. A true and correct copy of a fascimile from Daryl Winter of Genentech to Mr. Richman dated November 4, 1999 is attached hereto as Exhibit 2. Among other things, this Genentech communication indicates that because the "'co-expression of immunoglobin [sic] chains in recombinant host cells' patent has not yet been issued to Genentech . . . no royalty is due under that application." It is my understanding that this is a reference to the application that issued as United States Patent No. 6,331,415 (the "Cabilly II Patent") on December 18, 2001.

7. A true and correct copy of a letter from Joseph E. Panigot of MedImmune to Mr. Winter dated November 5, 1999 is attached hereto as Exhibit 3.

8. A true and correct copy of a Genentech Press Release dated on or about December 18, 2001 is attached hereto as Exhibit 4.

9. A true and correct copy of a letter from Sean A. Johnston of Genentech to Mr. Richman dated January 7, 2002 is attached hereto as Exhibit 5. This letter references a telephone conversation between Messrs. Johnston and Richman and notes that "[f]urther to [such] telephone conversation . . ., I am writing to confirm Genentech's expectation that MedImmune will pay royalties on sales of its Synagis® antibody product pursuant to the license granted by Genen-

tech under the recently issued U.S. Patent No. 6,331,415." The letter demanded that the royalties be paid "on or before March 1, 2002."

10. A true and correct copy of my letter to Mr. Johnston dated February 13, 2002 is attached hereto as Exhibit 6.

11. A true and correct copy of an article published in Nature Biotechnology dated February, 2002 is attached hereto as Exhibit 7.

12. Genentech did not respond to my February 13th letter by March 1, 2002, the date it demanded that the royalties be paid.

13. Based on, among other things, Mr. Johnston's January 7th letter, Genentech's refusal to respond to my February 13th letter by the date the royalty demand was due, Mr. Johnston's and Genentech's public statements about the breadth of the Cabilly II Patent, and obvious business realities, including, among other things, the dominant position of Genentech in the biotechnology industry (i.e., at that time it is my understanding that Genentech was one of the largest biotechnology companies in the United States) and the large amount of sales of MedImmune's Synagis® product, it was clear that Genentech would consider a failure by MedImmune to make royalty payments a material breach of the 1997 License Agreement, which would allow Genentech to terminate the agreement and sue MedImmune for patent infringement thereafter. MedImmune could do nothing to prevent Genentech from taking these actions, and it would have been logical for Genentech to do so.

14. A true and correct copy of my letter to Mr. Johnston dated March 8, 2002 is attached hereto as Exhibit 8.

15. A true and correct copy of Mr. Johnston's letter to me dated March 24, 2002 is attached hereto as Exhibit 9.

16. A true and correct copy of my letter to Mr. Johnston dated April 4, 2002 is attached hereto as Exhibit 10.

17. A true and correct copy of Mr. Johnston's letter to me dated May 16, 2002 is attached hereto as Exhibit 11.

18. A true and correct copy of my letter to Mr. Johnston dated May 23, 2002 is attached hereto as Exhibit 12.

* * *

I declare under penalty of perjury that the following is true and correct.

Dated: Gaithersburg, Maryland
March 29, 2004

/s/ William C. Bertrand
WILLIAM C. BERTRAND

[*Exhibit 1 to Bertrand Declaration*]

Genentech, Inc.

June 11, 1997

*Sent by Federal Express*

Michael Richman
Vice-President, Business Development
MedImmune, Inc.
35 West Watkins Mill Road
Gaithersburg, MD 20878

Dear Mike:

Enclosed please find a fully executed agreement between MedImmune and Genentech which grants a license to MedImmune under Genentech's Cabilly patents for antibodies binding the respiratory syncytial virus antigen.

As we discussed and agreed to, I would like to confirm that the royalty paid by MedImmune to the Medical Research Council for licenses to the Winter and Boss patents applies to Section 3.05(b) of the enclosed agreement regarding "Credits Against Royalties."

The license grant fee of $ . . . should be paid to Genentech within thirty days of your receipt of this agreement. Payment should be made by wire transfer according to the enclosed directions.

I would like to express my sincere appreciation for your efforts in completing this agreement, and I wish MedImmune the best in its development of antibodies to RSV.

With best regards,

/s/ Clint Rogers

CLINT ROGERS
Senior Analyst
Business and Corporate Development

Direct Telephone: (415) 225-6021
Direct Facsimile: (415) 225-3009
E-mail: *rogers.clint@gene.com*

GENENTECH, INC.

MAILING ADDRESS:

Genentech, Inc.
Treasury Department (Mail Stop 24)
460 Point San Bruno Boulevard
South San Francisco, CA 94080

FAX NUMBER:

(415) 225-2848

WIRE INSTRUCTIONS:

| | |
|---|---|
| Bank: | Citibank, N.A. |
| Address: | 399 Park Avenue<br>New York, NY 10043 |
| ABA Number: | 021-000-089 |
| Account Name: | Genentech, Inc. |
| Account Number: | 4052-7763 |

TAX I.D. NUMBER

94-2347624

This Agreement, dated as of June 4, 1997 is between Genentech, Inc., a Delaware corporation having a principal place of business at 460 Point San Bruno Blvd., South San Francisco, California 94080 (hereinafter "Genentech") and MedImmune, Inc. having a place of business at 35 West Watkins Road, Gaithersburg, Maryland 20878 (hereinafter "Licensee")

WHEREAS:

A. Genentech is the owner of certain patents and patent applications (patent rights) relating to methods and compositions in the field of immunoglobulins.

B. Genentech does not wish to have these patent rights hinder the development of immunoglobulin products and is willing to grant licenses for the development of products for public use and benefit as specified in this Agreement.

C. Licensee desires to obtain a license under the terms and conditions specified herein.

D. Genentech and Licensee believe that the subject matter of this license will be most effectively commercialized under conditions of limited exclusivity to encourage the investments required to develop and market such subject matter.

NOW, THEREFORE, the parties agree as follows:

## Article I

## DEFINITIONS

Unless otherwise specifically set forth herein, the following terms shall have the following meanings:

1.01. "Affiliate" of Licensee shall mean any entity that controls, is controlled by or is under common control with Licensee; and "control" for purposes of this definition shall mean the possession of the power to direct or cause the direc-

tion of the management and policies of an entity, whether through the ownership of voting stock, by contract or otherwise. In the case of a corporation, "control" shall mean the direct or indirect ownership of fifty percent (50%) or more of the outstanding voting stock together with a controlling membership on the board of directors of such corporation.

1.02. "Antigen" as used in this Agreement shall mean the respiratory syncytial virus (RSV) substance listed in Schedule A attached hereto and made a part of this Agreement. Schedule A may be amended from time to time by mutual agreement of the Parties in writing, at which time the financial terms pertaining to the newly added Antigen(s) may also be modified.

1.03. "Bulk Product" shall mean Licensed Product supplied in a form other than Finished Product which can be converted into Finished Product.

1.04. "Cost of Product" shall mean the cost of acquisition, if purchased, or the cost of manufacture, the latter being the sum of direct production costs and manufacturing overhead costs determined in accordance with generally accepted accounting principles.

1.05. "Designee" shall mean a person or entity designated by a Party to exercise the rights of and perform obligations hereunder in place of and to the exclusion of that Party in the Territory or a portion thereof.

1.06. "Effective Date" shall mean as to each Antigen, or Licensed Product based thereon, the later of the date of this Agreement or the date on which such Antigen was added to Schedule A by amendment.

1.07. "Field" shall mean the manufacture, use or sale of Licensed Product for the prevention or therapy of human diseases.

1.08. "Finished Product" shall mean any and all Licensed Products in form for use by an end user and not intended for further chemical or genetic manipulation or transformation.

1.09. "Licensed Patents" shall mean

(a) U.S. Patent No. 4,816,567 and the claims relating to chimeric antibodies found in patents or patent applications arising from divisionals, continuations or continuations-in-part of any application from which U.S. Patent No. 4,816,567 claims priority (excluding U.S.S.N. 07/205,419 and foreign counterparts thereof) as well as the foreign counterparts of the foregoing and any and all reissues, reexaminations or extensions of the foregoing ("Chimera Patents") and

(b) any patent issuing based on U.S.S.N. 07/205,419 (a continuation of the application maturing into U.S. Patent No. 4,816,567) relating to the coexpression of immunoglobulin chains in recombinant host cells, as well as the divisionals, continuations or continuations-in-part of such U.S.S.N. 07/205,419, the issued foreign counterparts of such U.S.S.N. 07/205,419 and any and all reissues, reexaminations or extensions of the foregoing ("Coexpression Patents"). Attached hereto as Schedule B is a list of patents and patent applications that Genentech in good faith believes represents Licensed Patents as of September 1, 1996. However no warranty is given as to the completeness or accuracy of Schedule B or any update thereof that might subsequently be provided to Licensee.

1.10. "Licensed Product(s)" shall mean the anti-RSV monoclonal antibody capable of binding to the Antigen listed in Schedule A hereto, the manufacture, use or sale of which substances would, if not licensed under this Agreement, infringe one or more claims of either or both of Chimera Patents or Coexpression Patents, which have neither expired nor been held invalid by a court or other body of competent jurisdiction from which no appeal has been or may be taken.

1.11. . . . .

1.12. "Party" shall mean Genentech or Licensee and when used in the plural shall mean Genentech and Licensee.

1.13. "Territory" shall mean the entire world.

## Article II

## GRANT

2.01. *License*. Subject to the fulfillment by Licensee of all the terms and conditions of this Agreement, Genentech hereby grants to Licensee and Licensee hereby accepts a coexclusive license together with the right to sublicense its Affiliates and Designees under Licensed Patents for the term thereof to make, use and sell Licensed Products in the Field and the Territory. This grant shall be coexclusive with Genentech, Inc., and additional licensees, if any, to be selected solely by Genentech. Genentech shall be free at its discretion to enter into agreements with such additional licensees at any time and on terms solely of its choosing. However, Genentech represents that, unless for a particular Antigen a different number of additional licenses is specified at the time such Antigen is included in Schedule A, it will not grant more than four (4) additional licenses in which both the Field and Territory are coextensive with that which is set forth herein.

2.02. *Right to Appoint Designee*. Licensee shall have the right to sublicense all of its rights hereunder for all or part of the Territory (including on a country-by-country basis) to a Designee of its choosing, to the exclusion of Licensee in such Territory or portion thereof, provided that Licensee agrees that it will indemnify Genentech for any failure of performance on the part of such Designee. An entity that simply acts to co-promote or to co-market Licensed Product supplied by Licensee shall not be considered a Designee and Licensee may co-promote or co-market such Licensed Product with such entity in a given country or countries, provided that (i) both Licensee and such entity obtain Licensed Products from the same manufacturing source, (ii) only one such entity shall be permitted to co-promote or co-market the same Licensed Product in a given country, and (iii) Licensee shall be responsible for the payment of royalties on Net Sales of

Licensed Products by such entity and for all other acts of such entity as if such acts were those of the Licensee.

2.03. *No Other License.* Licensee understands and agrees that no license under any patent or application other than Licensed Patents is or shall be deemed to have been granted under this Agreement, either expressly or by implication.

2.04. *Licenses Separately Available.* Licensee acknowledges that separate licenses under Chimera Patents and Coexpression Patents were available from Genentech upon request prior to entering into this Agreement, but that for reasons of convenience the licenses have been combined in this Agreement. Licensee further acknowledges that it was not coerced to enter into a license under either one of Chimera or Coexpression Patents as a condition to obtaining a license under the other, and that the licenses hereunder were not offered as a mandatory package.

## Article III

## FEES AND ROYALTIES

3.01. *License Grant Fee.* Within thirty (30) days after execution of this Agreement or amendment of Schedule A to add an Antigen thereto, Licensee shall pay to Genentech a non-creditable, non-refundable license grant fee of $ . . . per Antigen.

3.02. *Minimum Annual Royalties.* Licensee shall pay to Genentech a minimum annual royalty for each Antigen on or before January 31 of each year beginning with the third full

calendar year after the Effective Date for such Antigen in accordance with the following table:

| *Full Calendar Year* | *Minimum Annual Royalty* |
|---|---|
| 3 | $ . . . |
| 4 | $ . . . |
| 5 | $ . . . |
| 6 and each subsequent year | $ . . . |

Such payments shall be non-refundable but shall be creditable against earned royalties as provided in Section 3.05.

3.03. *Earned Royalties*. . . . .

3.04. *Sales To and Between Sublicensees*. . . . .

404
3.05. *Credits Against Royalties*. . . . .

3.06. *No Non-Monetary Consideration.* . . . .

3.07. *Most Favored Licensee.* . . . .

## Article IV

## RECORDS, REPORTS AND PAYMENTS

4.01. *Records Retention.* Licensee shall keep and shall cause its sublicensees to keep records of the sales of all Licensed Products in sufficient detail to permit Genentech to confirm the accuracy of Licensee's royalty calculations. At Genentech's request and expense, Licensee shall permit an independent certified public accountant appointed by Genentech and acceptable to Licensee to examine upon reasonable notice and at reasonable times, such records solely to the extent necessary to verify Licensee's calculations. Such examination shall be limited to a period of time no more than three (3) years immediately preceding the request for examination. If Licensee's royalties are found to be in error such that royalties to Genentech were underpaid by more than five (5) percent then Licensee shall promptly pay any deficiency, plus interest at the prime rate, to Genentech and reimburse Genentech for its costs in examining such records.

4.02. *Reports*. Within sixty (60) days after the end of each calendar quarter following Licensee's or its sublicensee's first sale of Licensed Product, Licensee shall furnish to Genentech a written report of all sales of Licensed Products subject to royalty under Section 3.03 during such calendar quarter. Such report shall include (i) the determination of Net Sales as specified in Section 1.11; (ii) detailed itemization of the credits taken pursuant to Section 3.05; and (iii) the royalty payment then due.

4.03. *Payments*. Concurrently with each report pursuant to Section 4.02, Licensee shall make the royalty payment then due. Payments shall be in United States dollars and, unless otherwise agreed in writing, shall be made by wire transfer to such bank as Genentech may from time to time designate in writing, without set-off and free and clear of and without any deduction or withholding for or on account of any taxes, duties, levies, imposts, fees or charges except .for withholding required by tax authorities for income taxes on royalties actually payable to Genentech after application of the credits permitted by Sections 3.05. Licensee shall make any withholding payments due on behalf of Genentech and shall promptly provide Genentech with official tax receipts or other written documentation sufficient to enable Genentech to satisfy the United States tax authorities with respect to Genentech's application for a foreign tax credit for such payment.

4.04. *Currency Conversion*. Royalties due on Net Sales of Licensed Products made in currency other than United States dollars shall first be calculated in the foreign currency and then converted to United States dollars on the basis of the rate of exchange in effect for purchase of dollars published in the *Wall Street Journal* on the last business day of the period for which royalties are due.

Article V

LIABILITY

5.01. *Indemnification.* Licensee shall defend, indemnify and hold Genentech harmless against any and all liability, damage, loss, cost or expense resulting from any third party claim, suit or other action arising out of or based on the manufacture, use or sale of any Licensed Product by Licensee, its sublicensees or co-promoting or co-marketing entities pursuant to Section 2.02: provided, however, that upon the filing of any such claim or suit, Genentech shall promptly notify Licensee and permit Licensee, at Licensee's cost, to handle and control such claim or suit and shall cooperate in the defense thereof.

Article VI

PATENT INFRINGEMENT

6.01. *Notification of Infringement.* Licensee shall notify Genentech of any infringement by third parties of any patent within Licensed Patents of which Licensee is aware and shall provide Genentech with the available evidence, if any, of such infringement.

6.02. *Enforcement of Licensed Patents.* . . . .

6.03. *No Warranty of Non-Infringement.* Nothing in this Agreement shall be construed as a representation made or warranty given by Genentech that the practice by Licensee or its sublicensees of the license granted hereunder will not infringe the patent rights of any third party.

## Article VII

## TERM AND TERMINATION

7.01. *Term.* This Agreement shall come into force as of its Effective Date and shall continue in full force and effect on a country-by-country basis unless earlier terminated as pro-

vided herein or until the expiration of the last to expire of the Licensed Patents.

7.02. *Termination for Breach.* Genentech shall have the right to terminate this Agreement and the licenses granted hereunder upon thirty (30) days' written notice to Licensee for Licensee's material breach of this Agreement if Licensee has failed to cure such breach within thirty (30) days of notice thereof.

7.03. *Insolvency.* Either Party may terminate this Agreement if, at any time, the other Party shall file in any court pursuant to any statute of any individual state or country, a petition in bankruptcy, insolvency or for reorganization or for an agreement among creditors or for the appointment of a receiver or trustee of the Party or of its assets, or if the other Party proposes a written agreement of composition or extension of its debts, or if the other Party shall be served with an involuntary petition against it filed in any insolvency proceeding, and such petition shall not be dismissed within sixty (60) days after the filing thereof, or if the other Party shall propose or be a Party to any dissolution or liquidation, or if the other Party shall make an assignment for the benefit of creditors.

7.04. *Termination by Licensee.* Licensee may terminate this Agreement in its entirety or with respect to one or more Antigens at any time upon six (6) months' written notice to Genentech.

7.05. *Effect of Termination.* Termination of this Agreement in whole or in part for any reason shall not relieve Licensee of its obligations to pay all fees and royalties that shall have accrued hereunder prior to the effective date of termination. Termination of this Agreement as to Licensee shall result in the termination of the licenses of Licensee and all sublicensees of Licensee. The provisions of Sections 2.04 and 3.08 shall survive termination of the Agreement for any reason except termination for breach by Genentech.

## Article VIII

## MISCELLANEOUS PROVISIONS

8.01. *Limitations on Assignments.* Neither this Agreement nor any interests hereunder shall be assignable by either Party without the written consent of the other; provided, however, that either Party may assign this Agreement to any corporation or entity with which it may merge or consolidate, or to which it may transfer substantially all of its assets or all of its assets to which this Agreement relates without obtaining the consent of the other Party.

8.02. *Jurisdiction and Choice of Laws.* This Agreement shall be interpreted and construed under the laws of California, and Licensee agrees to submit to the jurisdiction of California.

8.03. *Relationship of the Parties.* Nothing in this Agreement is intended or shall be deemed to constitute a partnership, agency, employer-employee, or joint venture relationship between the Parties.

8.04. *Further Acts and Instruments.* Each Party hereto agrees to execute, acknowledge and deliver such further instruments and to do all such other acts as may be necessary or appropriate to effect the purpose and intent of this Agreement.

8.05. *Entire Agreement.* This Agreement constitutes and contains the entire agreement of the Parties and supersedes any and all prior negotiations, correspondence, understandings and agreements between the Parties respecting the subject matter hereof. This Agreement may be amended or modified or one or more provisions thereof waived only by a written instrument signed by the Parties.

8.06. *Severability.* If in any jurisdiction any one or more of the provisions of this Agreement should for any reason be held by any court or authority having jurisdiction over this Agreement or any of the Parties hereto to be invalid, illegal or

unenforceable, such provision or provisions shall be validly reformed to as nearly approximate the intent of the Parties as possible and if unreformable, the Parties shall meet to discuss what steps should be taken to remedy the situation; in other jurisdictions, this Agreement shall not be affected.

8.07. *Captions*. The captions to this Agreement are for convenience only and are to be of no force or effect in construing and interpreting the provisions of this Agreement.

8.08. *WARRANTIES*. The Parties represent and warrant that they have the power to enter into this agreement. OTHERWISE, THE PARTIES EXPRESSLY DISCLAIM ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT.

8.09. *Notices*. Any notice, request, approval or other document required or permitted to be given under this Agreement shall be in writing and shall be deemed to have been sufficiently given when delivered in person, transmitted by telex, telecopier, telegraph or deposited in the mail, postage prepaid, for mailing by first class, certified or registered mail, return receipt requested, addressed as follows:

If to Licensee, addressed to:

MedImmune, Inc.
35 West Watkins Mill Road
Gaithersburg, MD 20878
Attn.: Chief Executive Officer

If to Genentech, addressed to:

Genentech, Inc.
460 Point San Bruno Boulevard
South San Francisco, CA 94080
Attn: Corporate Secretary

or to such other address or addresses as may be specified from time to time in a written notice.

8.10. *Wire Transfer of Funds.* Unless otherwise specified in writing, all payments by Licensee required hereunder shall be made by wire transfer at the direction of Genentech.

IN WITNESS WHEREOF, Genentech and Licensee have caused this Agreement to be executed by their duly authorized representatives.

MEDIMMUNE, INC.

By: /s/ David M. Mott

Title: President & C.O.O.

Date: 6/2/97

GENENTECH, INC.

By: /s/ [illegible]

Title: Vice President

Date: 6/5/97

Schedule A

Antigens

[Redaction]

# SCHEDULE B

## Patents and Patent Applications

[Redaction]

[*Exhibit 2 to Bertrand Declaration*]

GENENTECH, INC.
BUSINESS AND CORPORATE DEVELOPMENT

FACSIMILE TRANSMITTAL SHEET

| TO | FROM |
|---|---|
| Michael Richman | Daryl Winter |
| COMPANY. | DATE |
| MedImmune, Inc. | 11/04/99 |
| RE | TOTAL NO OF PAGES INCLUDING COVER |
| Cabilly License | 1 |
| PHONE NUMBER | PHONE NUMBER |
| 301-527-4454 | 650-225-1249 |
| FAX NUMBER | FAX NUMBER |
| 301-527-4201 | 650-225-3009 |

Dear Michael:

Based on our recent discussions, it is my understanding that MedImmune does not intend to take a Cabilly license for MEDI-507 (anti-CD2) at this time. Please keep in mind that the availability of a license for a particular antigen depends, among other things, on the demand by other companies for license to that antigen, and as such, we can not guarantee that licenses will be available in the future. . . . .

On a separate but related matter, I have reviewed our license with MedImmune dated June 4, 1997. According to our Finance department, no quarterly payments or reports have been submitted regarding payment of Royalties on New Sales of Synagis, anti RSV, since this product has been marketed.

While the "co-expression of immunoglobin chains in recombinant host cells" patent has not yet been issued to Genentech, and thus under § 1.10, no royalty is due under that application, U.S. Patent 4,815,567 related to chimeric antibodies is in force and accordingly we believe. . . . .

Please advise us of the reasons for the absence of quarterly reports and royalty payments. Your prompt response to this inquiry would be most appreciated.

Should you have any questions on either of the issues mentioned above, please do not hesitate to contact me.

Regards,

/s/ Daryl Winter

[*Exhibit 3 to Bertrand Declaration*]

[Logo]

MedImmune, Inc.

November 5, 1999

Daryl Winter
Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080

Dear Mr. Winter:

In response to the communication you faxed earlier today, I would like to take the opportunity to ensure that our intent in obtaining a license for the Cabilly patent is not misunderstood. Although I had previously expressed concerns regarding the financial terms being offered, we are still nonetheless interested in licensing this patent. I will contact you subsequently to discuss this further.

I would also like to respond to your analysis of MedImmune's royalty obligation concerning US Patent 4,816,567 (the '567 Patent). MedImmune has consistently maintained that due to its humanized nature, Synagis® falls outside the claims of chimeric antibody patents. Thus, we do not believe that there is a royalty obligation to Genentech based upon the '567 patent.

I hope these explanations are helpful. If you have any questions or concerns regarding these matters, please do not hesitate to contact me.

Sincerely,

/s/ Joseph E. Panigot
JOSEPH E. PANIGOT
Associate director, Business Development

cc: Michael Richman

[*Exhibit 4 to Bertrand Declaration*]

Genentech, Inc.

[Logo]

NEWS
PRESS RELEASE

Genentech Granted Fundamental U.S.
Patent for Antibody Technology

SOUTH SAN FRANCISCO, Calif.—December 18, 2001—Genentech, Inc. (NYSE: DNA) announced that the United States Patent and Trademark Office today granted U.S. Patent No. 6,331,415 relating to fundamental methods and compositions used to produce antibodies by recombinant DNA technology.

This patent, which has clams for the co-expression of antibody heavy and light chains, covers a principal way that therapeutic and diagnostic antibodies are made by biotechnology and pharmaceutical companies and others using recombinant DNA technology. Examples of such antibodies at Genentech include the Herceptin® antibody product for the treatment of certain forms of HER-2 overexpressing metastatic breast cancer, and the Rituxan® antibody product for the treatment of certain forms of B-cell non-Hodgkin's lymphoma. Genentech has a number of existing licensing agreements in place that grant rights under this patent to other companies for certain other antibodies developed by those companies. Genentech expects that a number of additional companies will seek licenses under the patent.

The patent is based on a collaboration between scientists at Genentech and at the City of Hope National Medical Center in the early 1980s, and it is the second U.S. Patent to result from that collaboration. The patent is unrelated to recent contract disputes between Genentech and the City of Hope. The patent granted today follows almost ten years of

proceedings in the Patent Office and in the United States District Court to determine whether the invention covered by the patent was invented first by scientists at Genentech and City of Hope or by scientists at Celltech in England. Earlier this year, following a court-ordered mediation that resulted in an agreement between Genentech and Celltech to settle the priority dispute, the court determined that Genentech was entitled as a matter of law to priority over Celltech and accordingly, that Genentech should be awarded the patent on the invention. Following that determination, the Patent Office again independently examined Genentech's patent application and concluded that the patent should issue.

Genentech, Inc. is a leading biotechnology company that discovers, develops, manufactures and markets human pharmaceuticals for significant unmet medical needs. Fifteen of the currently approved biotechnology products stem from or are based on Genentech science. Genentech markets ten biotechnology products directly in the United States. The company has headquarters in South San Francisco, Calif. and is traded on the New York Stock Exchange under the symbol DNA.

[*Exhibit 5 to Bertrand Declaration*]

Genentech, Inc.

LEGAL DEPARTMENT
1 DNA Way
South San Francisco, CA 91080-4990
(650) 225-1000
FAX (650) 952-9881 or (650) 952-9882

January 7, 2002

*VIA FEDERAL EXPRESS*
Michael S. Richman
Senior Vice-President, Corporate Development
and Administration
MedImmune, Inc.
35 West Watkins Mill Road
Gaithersburg, MD 20878

Dear Mike:

Further to our telephone conversation a couple of weeks ago, I am writing to confirm Genentech's expectation that MedImmune will pay royalties on sales of its Synagis® antibody product pursuant to the license granted by Genentech under the recently issued U.S. Patent No. 6,331,415.

According to the license Agreement between our companies dated June 4, 1997, the royalty owed for the license under the '415 patent is. . . . . Royalty payments are due on a quarterly basis, within sixty days following the end of each calendar quarter. Because the '415 patent issued on December 18, 2001 the first royalty payment will be due on or before March 1, 2002.

Should you have any questions regarding this matter, please do not hesitate to contact me.

Very truly yours,
GENENTECH, INC.

/s/ Sean Johnston
SEAN A. JOHNSTON
Vice President, Intellectual Property

[*Exhibit 6 to Bertrand Declaration*]

[Logo]

MedImmune, Inc.

February 13, 2002

*BY TELECOPIER*

Sean A. Johnston, Esq.
Vice President, Intellectual Property
Genentech, Inc.
Legal Department
1 DNA Way
South San Francisco, CA 94080-4990

Dear Sean:

This is in response to your January 7, 2002 letter to Michael Richman regarding Genentech's U.S. Patent No. 6,331,415 (the "'415 Patent").

While we understand that Genentech has an "expectation that MedImmune will pay royalties on sales of Its Synagisa® antibody product pursuant to the license [Agreement dated June 4, 1997 (the "Agreement")]," it would be helpful if you could please advise us as to your basis for believing that MedImmune's product would infringe any valid claim of the '415 Patent such that royalties would be due.

In addition, we would appreciate it if you could give us a copy of the settlement agreement entered into between Genentech and Celltech R&D, Inc. which resulted in the issuance of the '415 Patent (and the revocation of the Boss patent, to which MedImmune has a license), the interference file itself, as well as the documentary evidence that was cited by the U.S. District Court for the Northern District of California as the reason for the settlement agreement giving the '415 Patent priority over the now-revoked Boss patent.

Finally, as you know, the Agreement is now drafted to cover products binding to antigens listed in Schedule A, which currently include "[a]ntigens expressed by respiratory syncytial virus . . . ." We have previously inquired about the possibility of adding additional antigens to Schedule A (as contemplated by Section 1.02 of the Agreement) and you advised us that Genentech had not, as of that time, reached a decision on this matter and on its licensing policy with respect to the '415 Patent generally. We trust that by now Genentech has determined its position and we would appreciate your advising us of it. In particular, without conceding that such a license would be required, we are interested in knowing whether Genentech is willing to provide MedImmune with a license under the '415 Patent for the following MedImmune products under development: (1) Medi-507 (anti-CD2 antibody); (2) Vitaxin (TM) (anti $\alpha_1\beta_3$ antibody); (3) antibodies against IL-9 (or IL-9 receptor) and (4) antibodies against EphA2.

Thank you in advance for your help and cooperation.

Very truly yours,

/s/ William C. Bertrand, Jr.
WILLIAM C. BERTRAND, JR.
Vice President, Legal Affairs

[*Exhibit 7 to Bertrand Declaration*]

*Nature Biotechnology*, February 2002, p. 108

Genentech awarded critical antibody patent

In December 2001, after a more than decade-long dispute over inventorship with Celltech R&D Ltd (Slough, UK), the biotech giant Genentech (S. San Francisco, CA) was awarded a patent claiming broad rights to fundamental methods for the recombinant expression of antibodies. The patent covers one of the principal processes used in the manufacturing of lucrative therapeutic and diagnostic antibody drugs, such as Genentech's breast-cancer therapeutic Herceptin, and could potentially block the production of antibody products by rival companies or increase their royalty burden.

Genentech's US Patent No. 6,331,415 ("Cabilly patent"), which was awarded on December 18, is a continuation of a previously issued Cabilly patent filed by Genentech on April 8, 1983 as part of a collaborative effort between Genentech and the City of Hope National Medical Center (Duarte, CA). The newly issued patent has 36 claims for recombinant methods and vectors to produce immunoglobulin (Ig) molecules and functionally Ig fragments in transformed host cells.

Genentech's application was on file with the US Patent and Trademark Office (PTO; Washington DC) when Celltech's US patent 4,816,397 ("Boss patent"), covering the same patentable invention, was granted in March 1989, having been filed on March 24, 1983. In February 1991, after the issuance of the Boss patent, Genentech asked the Board of Patent Appeals and Interferences to begin an interference action to determine which of the two companies had rights to the invention.

Seven years later in August 1998, a panel of administrative patent judges found in favor of Celltech, criticizing the evidentiary value of the Genentech inventor's notebooks and corroborating evidence. Genentech responded by filing suit

A court-ordered settlement—required by the US District Court before it would render its decision on inventorship—provides Celltech with a license to the Genentech patent to continue its R&D activities in return for an undisclosed royalty on future product sales. Notably, Genentech will pay Celltech for any lost income it would have generated from increasing revenue or the sales of any products covered by the Boss patent, which would have expired in 2006.

Meanwhile, Genentech believes that issuance of the Cabilly patents could affect many companies. "The recently issued patent broadly covers the co-expression of immunoglobulin heavy and light chain genes in a single host cell," says Sean Johnston, Genentech's vice president of intellectual property. "We do not believe that the claims are limited by type of antibody (murine humanized [90% human sequence], or human) or by host cell type."

Leading antibody companies, such as IDEC (San Diego, CA), Abgenix (Freemont, CA), and Medarex (Princeton, NJ) are now comparing their technologies with the issued patent claims to determine whether they need a license from, or should pay royalties on current products to, Genentech. And Celltech licensees—such as ImClone Systems (New York), which is co-developing an anti-cancer drug with Bristol

Myers Squibb—may now need to go to Genentech for a license. Some suggest that if licensing and royalty payments are owed, there will be corresponding increase in the production costs of those therapeutic and diagnostic antibodies. But Genentech disagrees. "Any increased cost depends largely on the particular antibody, the technology used to produce the antibody, and how many of those steps need to be licensed," says Johnston.

Investors are also scrambling to determine whether companies will now need to pay unanticipated royalties. "This patent aroused our interest because there are 11 antibody-based drugs on the market and over 90 additional products under development at various biotechnology companies," says BancAmerica Securities (New York) biotechnology analyst Thomas McGahren. "We have reviewed this patent and consider it to be very important, and companies producing chimeric or humanized antibodies will have to review carefully and determine if they need a license," says McGahren. "From an investment perspective, we are interested whether companies, such as MedImmune, will need a license or pay royalties on this essentially basic genetic engineering technology because they produce humanized antibodies," he adds. "Medarex and Abgenics, which produce human antibodies, may not have to face additional royalty and licensing feet."

*Debra Robertson, San Diego, CA*

[*Exhibit 8 to Bertrand Declaration*]

[Logo]

MedImmune, Inc.

March 8, 2002

BY TELECOPIER

Sean A. Johnston, Esq.
Vice President, Intellectual Property
Genentech, Inc.
Legal Department
1 DNA Way
South San Francisco, CA 94080-4990

Dear Sean:

This is a follow-up to our letter of February 13, 2002, which responded to your January 7, 2002 letter to Michael Richman regarding Genentech's U.S. Patent No. 6,331,415 B1 (the "'415 Patent").

To date, we have not yet received any response to the questions we asked in our February 13th letter. As we then indicated, we require responses to our inquiries and the documents we requested in order to evaluate your claim that MedImmune owes royalties to you pursuant to our June 4, 1997 agreement. As you know we wired you a payment on March 4, 2002 in the amount of $ . . . . Such payment, however, was made under protest and with reservation of all of our rights. We expect an answer to our questions immediately so that we may evaluate how further to proceed.

Very truly yours,

/s/ William C. Bertrand, Jr.
WILLIAM C. BERTRAND, JR.
Vice President, Legal Affairs

[*Exhibit 9 to Bertrand Declaration*]

Genentech, Inc.

LEGAL DEPARTMENT
1 DNA Way
South San Francisco, CA 94080-4990
(650) 225-1000
FAX (650) 952-9881 or (650) 952-9882

March 24, 2002

VIA FACSIMILE (301)527-4214
William C. Bertrand, Jr.. Esq.
Vice President, Legal Affairs
MedImmune, Inc.
35 West Watkins Mill Road
Gaithersburg, MD 20878

Re: Agreement between Genentech and MedImmune dated June 4, 1997

Dear Bill:

I am writing in response to your letter to me dated February 13, 2002, regarding Genentech's U.S. Patent No. 6,331,415, under which MedImmune currently has a license to make, use, and sell its Synagis® humanized monoclonal antibody product.

The United States Patent and Trademark Office ("PTO") issued the '415 patent to Genentech after litigation in the United States District Court to resolve the issue of whether Genentech or Celltech Therapeutics had priority to the claimed invention. The District Court issued findings of fact and conclusions of law that Genentech had, as a matter of law, established and was entitled to priority. After the District Court issued those findings and conclusions, Genentech filed with the PTO voluminous documents including (a) all pleadings filed in the District Court action, (b) transcripts of all depositions, including exhibits, taken in the District Court

action, (c) all documents produced in the District Court action, and (d) Genentech's settlement agreement with Celltech. The PTO thereafter independently examined Genentech's pending application and concluded that it met all of the requirements of patentability under the United States Code. The PTO also cancelled the claims of Celltech's U.S. Patent No. 4,816,397.

Your letter asks for the basis of Genentech's belief that MedImmune's Synagis product is within the scope of the claims of the '415 patent. Our belief is based primarily on our understanding that Synagis is an immunoglobulin molecule composed of heavy and light claims (each chain including a variable domain) that is produced by a process that involves the use of certain recombinant DNA technology to co-express the heavy and light chains in a single host cell. If our understanding is incorrect, please let us know in what respect it is incorrect, and what the correct information is regarding the structure of Synagis and/or the process by which it is produced, so that we may reevaluate our position.

Your letter states that "it would be helpful" to know the basis of Genentech's belief that is MedImmune's Synagis product is within the scope of the claims of the '415 patent. Obviously, however, MedImmune is able to evaluate for itself whether it believes the Synagis product is within the scope of the claims of the '415 patent. In this regard, we note with appreciation MedImmune's March 4, 2002 royalty payment, under the '415 patent, on sales of Synagis.

Your letter also asks for numerous documents, including the settlement agreement between Genentech and Celltech. The settlement agreement is a confidential document, and we cannot provide it to you. The documents you have requested are amongst those that Genentech filed with the PTO before the '415 patent issued, and, as noted above, both the District Court and the PTO concluded based on all the evidence that Genentech was entitled to the '415 patent. We do not believe

that the documents you have requested are relevant to the question of whether or why MedImmune must pay Genentech further royalties. Nevertheless, if there are a few specific documents from the prosecution of the '415 patent, the interference proceeding in the PTO, or from the litigation in the District Court that you would like to review, please let us know which ones those are and we will try to provide copies of them to you from our own files. Because the complete set of such documents is voluminous, if you wish to review more than just a few, you should obtain copies of the documents directly from the PTO, as allowed by law.

Finally, your letter asks whether, and under what terms, Genentech would be willing to grant MedImmune a license under the '415 patent for various antibody products that MedImmune has under development. We appreciate MedImmune's interest in additional licenses under the '415 patent, and hope to be able to respond to you shortly. We look forward to continuing our commercial relationship.

Very truly yours,

GENENTECH, INC.

/s/ Sean Johnston
SEAN A. JOHNSTON
Vice President, Intellectual Property

[*Exhibit 10 to Bertrand Declaration*]

[Logo]

MedImmune, Inc.
April 4, 2002

VIA FACSIMILE

Sean A. Johnston, Esq.
Vice President, Intellectual Properly
Legal Department
Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080-1990

Re: Genentech's U.S. Patent No. 6,331,415 ("'415 Patent")

Dear Sean:

We have your letter dated March 24, 2002 relating to the '415 Patent.

We are disappointed by your refusal to provide us with a copy of the settlement agreement entered into between Genentech and Celltech R&D, Inc. which resulted in the issuance of the '415 Patent as well as the documentary evidence that was cited by the U.S. District Court for the Northern District of California as the reason for the settlement agreement giving the '415 Patent priority over the now-revoked Boss patent.

Your letter states that after the District Court order announcing the settlement, "Genentech filed with the PTO voluminous documents including (a) all pleadings filed in the District Court action, (b) transcripts of all depositions, including exhibits, taken in the District Court action, (c) all documents produced in the District Court action, and (d) Genentech's settlement agreement with Celltech." However, there is no reference to any of these materials in the docket sheets for either the Interference file or the '415 Patent prosecution file.

If you would tell us where and when these materials were filed that would be helpful.

Assuming these materials are at the PTO, are we correct in our understanding that you have no objection to the PTO making them available to us? If so, we would appreciate a letter to that effect. If you do object for some reason, please advise us of that. As I am sure you understand, given your assertion that MedImmune's Synagis® product is within the scope of the claims of the '415 Patent (an assertion that we will not respond to before we have completed our analysis) we have an obvious interest in the terms of the settlement agreement and the other requested documents and are unaware of any good-faith basis for your claim of confidentiality.

Finally, assuming that the '415 patent is valid, enforceable and that MedImmune would require a license under such patent for various MedImmune products under development, we note that you have not answered our question of whether Genentech would be willing to provide such licenses, other than to note that you "hope to be able to respond . . . shortly." Without conceding coverage of any particular product in development, Genentech's licensing policy with respect to the '415 patent has the potential to be a significant factor in MedImmune's research and development strategies. Thus, please advise when such a response can be expected.

Very truly yours,

/s/ William C. Bertrand, Jr.
WILLIAM C. BERTRAND, JR.
Vice President, Legal Affairs

*[Exhibit 11 to Bertrand Declaration]*

Genentech, Inc.

LEGAL DEPARTMENT
1 DNA Way
South San Francisco, CA 94080-4990
(650) 225-1000
FAX (650) 952-9881 or (650) 952-9882

May 16, 2002

VIA FEDERAL EXPRESS
COPY (w/o enclosure) VIA FACSIMILE (301) 527-4214
(2 PAGES)
William C. Bertrand, Jr., Esq.
Vice President, Legal Affairs
MedImmune, Inc.
35 West Watkins Mill Road
Gaithersburg, MD 20878

Re: Agreement between Genentech and MedImmune dated June 4, 1997

Dear Bill:

We write in response to your letter dated April 4, 2002 regarding our U.S. Patent No. 6,331,415.

Your letter states that you are having trouble locating the documents referred to in our letter of March 24, 2002. We filed those documents with the PTO on or about September 13, 2001, and we enclose for your reference a copy of the PTO Form 1449 that accompanied the documents when they were filed. As you will see, the Form 1449 was initialed and signed by Examiner Gambel, indicating that the documents were indeed received by the PTO and fully considered by the Examiner prior to the issuance of the '415 patent.

We trust that this additional information will allow you now to locate and to obtain copies of the documents that you are interested in and that are publicly available from the PTO. Like any member of the public, you are free to obtain copies

of publicly available documents directly from the PTO by making a request to the PTO in accordance with its rules and regulations. No letter of permission or authorization from us it required. As we believe you already are aware, however, the settlement agreement between Genentech and Celltech is not publicly available from the PTO. The settlement agreement is a confidential business document that the rules and regulations of the PTO clearly allow to be kept confidential (37 CFR 1.666(b)).

Furthermore, the settlement agreement is not relevant to the issues of the scope of claims of the '415 patent, or whether Genentech's a patent application met the requirements of U.S. law for the issuance of a patent. The PTO independently determined that Genentech's application did meet all of those requirements. We note that you have not given any explanation in either your April 4 letter or your previous correspondence as to why the settlement agreement is relevant to the question of whether or why MedImmune's Synagis® product is within the scope of the claims of the '415 patent.

Regarding MedImmune's interest in obtaining additional licenses under the '415 patent for various MedImmune products in development (identified in your February 13, 2002 letter), we are willing to meet with MedImmune representatives to discuss the availability of and terms for possible licenses for those products. If you would please let us know several dates when MedImmune representatives would be available for such a meeting, we can proceed with scheduling. We look forward to hearing from you, and to continuing our commercial relationship with MedImmune.

Very truly yours,

GENENTECH, INC.

/s/ Sean Johnston
SEAN A. JOHNSTON
Vice President, Intellectual Property

[enclosure omitted in printing]

[*Exhibit 12 to Bertrand Declaration*]

[Logo]

MedImmune, Inc.
May 23, 2002

VIA FACSIMILE: 650.952.9881

Sean A. Johnston, Esq.
Vice President, Intellectual Properly
Genentech, Inc.
Legal Department
1 DNA Way
South San Francisco, CA 94080-4990

Re: U.S. Patent No. 6,331,415 B1 ("'415 Patent")

Dear Sean:

We write in response to your letter dated May 16, 2002 with respect to the '415 Patent.

First, we are happy to meet with you to discuss whether Genentech is willing to license various MedImmune products in development on commercially reasonable terms. Specifically, we could be available to meet with you in early July (we are in the process of retaining a new head of Business Development and I would like that person to join us). I would propose a meeting any day during the week of July 8. While we do not set this as a pre-condition to any such meeting, we would again ask you to make available to MedImmune a copy of the settlement agreement that resulted in the issuance of the '415 Patent. As the Patent relates to technology that is about twenty years old, we do not understand how there could be any confidentiality issue. Moreover, contrary to your suggestion that the settlement agreement is irrelevant to the patent or our negotiations, we believe that it may very well be pertinent to our obligations, if any, with respect to the '415 Patent, given that the settlement agreement essentially forms the basis for the issuance of the patent.

Second, we appreciate your enclosing a copy of PTO Form 1449 which you say was filed with the PTO "on or about September 13, 2001." We note, however, that while the form appears to be dated by examiner Gambel on October 5, 2001, it does not indicate that it was filed "on or about September 13, 2001." We would appreciate seeing any documentation or information you could give us that would help us establish the actual filing date. Moreover, given that the settlement agreement does not appear to be included as any of the items on the Form 1449, we would also appreciate any documentation indicating when and where such agreement was filed.

We look forward to a meeting at your earliest convenience. Please let me know if we can schedule a meeting some time during the week of July 8.

Very truly yours,

/s/ William C. Bertrand, Jr.
WILLIAM C. BERTRAND, JR.
Vice President, Legal Affairs

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed Apr. 30, 2004]

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Case No. CV03-2567 MRP (CTx)

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MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

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ENTRY OF JUDGMENT

For the reasons set forth in the Amended Memorandum of Decision and Order Re Motion to Dismiss for Lack of Subject Matter Jurisdiction, this Court enters final judgment on the first, second, third and fourth causes of action and hereby dismisses those claims as to both Genentech, Inc. and City of Hope. All claims and all defendants are hereby dismissed. This Order is a final judgment for purposes of Fed. R. Civ. P. 54(a). It shall be entered pursuant to Fed. R. Civ. P. 58 and 79(a), and served upon the parties.

IT IS SO ORDERED.

DATED: April 29, 2004 /s/ Mariana R. Pfaelzer
Honorable Mariana R. Pfaelzer
United States District Judge

# NON-EXCLUSIVE CABILLY PATENT LICENSE AGREEMENT

[Cabilly Coexpression Patents]

This Non-Exclusive Cabilly Patent License Agreement ("Agreement") is effective as of January 29, 2003 ("Effective Date") by and between Genentech, Inc., a Delaware corporation having its principal place of business at 1 DNA Way, South San Francisco, California 94080 (hereinafter "Genentech") and MedImmune, Inc., a Delaware corporation having its principal place of business at 35 West Watkins Mill Road, Gaithersburg, MD 20878 (hereinafter "Licensee").

WHEREAS:

A. Genentech owns and controls certain patent rights relating to methods and compositions in the field of antibodies (the "Licensed Patents", as that term is defined below);

B. Licensee is developing, and intends to commercialize, antibody products that bind to T-cell surface antigen CD2 ("CD2") and wishes to acquire a non-exclusive license for such products under the Licensed Patents; and

C. Genentech is willing to grant such a non-exclusive license to Licensee on the terms and conditions set forth below.

NOW, THEREFORE, in consideration of the promises and the mutual covenants recited herein, the Parties agree as follows:

## Article I

## DEFINITIONS

Unless otherwise specifically set forth herein, the following terms shall have the following meanings:

1.01. "Affiliate" with respect to Licensee shall mean any corporation or other entity which, directly or indirectly, controls, is controlled by or is under common control with, a Party. For the purpose of this Section 1.01 "control" shall mean (i) the ownership, directly or indirectly, of at least fifty percent (50%) of the outstanding voting securities or other ownership interest of an entity, or (ii) the possession, directly or indirectly, of the power to manage, direct or cause the direction of the management and policies of the corporation or other entity or the power to elect or appoint fifty percent (50%) or more of the members of the governing body of the corporation or other entity.

1.02. "Bulk Product" shall mean Licensed Product supplied in a form other than Finished Product which can be converted into Finished Product.

1.03. "Calendar Quarter" shall mean each three month period commencing January 1, April 1, July 1 and October 1 of each year during the term of this Agreement.

1.04. "Chimera Patents" shall mean (i) U.S. Patent No. 4,816,567, issued March 28, 1989 from U.S. patent application serial no. (USSN) 06/483,457, and (ii) any claims specifically directed to chimeric antibodies or any method of making or using chimeric antibodies, which claims are found in any patent(s) issuing from divisionals, continuations, or continuations-in-part of any application from which U.S. Patent No. 4,816,567 claims priority, (iii) any claims specifically directed to chimeric antibodies or any method of making or using chimeric antibodies, which claims are found in any patents that are reissues, reexaminations, or extensions

of any of the foregoing (i) and (ii), and (iv) foreign counterparts of any of the foregoing (i), (ii), or (iii).

1.05. "Cost of Product" shall mean the cost of acquisition, if purchased, or the cost of manufacture, the latter being the sum of direct production costs and manufacturing overhead costs determined in accordance with U.S. Generally Accepted Accounting Principles ("GAAP").

1.06. "Designee" shall mean a corporation or other entity that is licensed by Licensee to exercise the rights of Licensee hereunder in concert with, or in place of and to the exclusion of, Licensee in all or part of the Territory on a country-by-country basis.

1.07. "Field of Use" shall mean the prevention or therapy of human disease.

1.08. "Finished Product" shall mean any and all Licensed Product in a form for use by an end user and not intended for further chemical or genetic manipulation or transformation.

1.09 "First Commercial Sale" shall mean the first sale of any Licensed Product by Licensee or any of its Affiliates or Designees to a non-affiliated third party. The sale shall be deemed to occur on the earlier of (i) the date the Licensed Product is shipped to the third party, or (ii) the date of the invoice to the third party for the Licensed Product.

1.10. "Licensed Patents" shall mean (i) U.S. Patent No. 6,331,415, issued December 18, 2001, (ii) any patent(s) issuing from divisionals, continuations, or continuations-in-part of any patent application from which U.S. Patent No. 6,331,415 claims priority, and (iii) patents that are reissues, reexaminations, extensions, or foreign counterparts of any of the foregoing (i) or (ii), provided, however, that Licensed Patents shall not include Chimera Patents.

1.11. "Licensed Product" shall mean any antibody that binds specifically to CD2, the making (or having made),

using, selling, offering for sale or importing of which, but for the license granted under this Agreement, would infringe a Valid Claim of a patent included in Licensed Patents.

[Redaction]

1.13. "Party" shall mean either Genentech or Licensee, and when used in the plural shall mean both Genentech and Licensee.

1.14. "Term" is defined in Section 7.01.

1.15. "Territory" shall mean the entire world.

1.16. "U.S." and "United States" shall mean the United States of America, including its territories and possessions.

1.17. "Valid Claim" shall mean any claim of an issued and unexpired patent within the Licensed Patents that has not been disclaimed, abandoned or dedicated to the public or held unenforceable, unpatentable or invalid by a decision of a court or governmental agency of competent jurisdiction, which decision is unappealable or unappealed within the time allowed for appeal.

## Article II

## GRANT

2.01. *License*. Genentech hereby grants to Licensee and Licensee hereby accepts a nonexclusive license under Licensed Patents during the Term to make (and have made), use, sell, offer for sale, and import Licensed Product in the Territory in the Field of Use. Licensee shall have a limited right to grant sublicenses as provided in Section 2.02.

2.02. *Right to Grant Sublicenses*. Licensee shall only have the right to grant sublicenses to its Affiliates and Designees of the rights granted hereunder to Licensee to make (and have made), use, sell, offer for sale, and import Licensed Product, in all or part of the Territory on a country-by-country basis; provided that Licensee shall always be responsible for the payment of royalties on Net Sales of Licensed Product by any such sublicensee and for all other acts of such sublicensee as if such acts were those of the Licensee. A sublicense granted under this Section 2.02 shall not be further sublicensable or sublicensed by the licensee thereof.

2.03. *No Other License.* Licensee understands and agrees that no license under any patent or patent application other than Licensed Patents, or under any know-how, is or shall be deemed to have been granted under this Agreement, either expressly or by implication. By way of example only, and without limitation, no license under Chimera Patents is granted hereunder.

## Article III

## FEES, MILESTONES AND ROYALTIES

3.01. *License Grant Fee.* Within ten (10) business days after the Effective Date, Licensee shall pay to Genentech a non-creditable, non-refundable license grant fee of . . . dollars (U.S. $ . . .).

3.02. *Development Milestone Fee.* Within ten (10) business days after receipt by Licensee of the first marketing approval for a Licensed Product from the United States Food and Drug Administration or any successor agency or authority thereto ("FDA"), Licensee shall pay to Genentech a non-creditable, non-refundable development milestone fee of $ . . . dollars (U.S. $ . . .).

3.03. *Earned Royalties.* . . . .

3.04. *Sales To or Between Licensee, Affiliates, and Designees.* . . . .

3.05. *No Non-Monetary Consideration.* . . . .

3.06. *No Credit Against Royalties.* . . . .

## Article IV

## RECORDS, REPORTS AND PAYMENTS

4.01. *Records Retention.* Licensee shall keep and shall cause its Affiliates and Designees to keep true, complete and accurate records of all sales of all Licensed Product in accordance with GAAP, or the equivalent, and in sufficient detail to permit Genentech to confirm the accuracy of Licensee's royalty calculations. At Genentech's request and expense, Licensee shall permit not more than once in a twelve (12) month period an independent certified public accountant appointed by Genentech and acceptable to Licensee to examine at Licensee's principal place of business, upon reasonable notice and at reasonable times, such records solely to the extent necessary to verify Licensee's calculations. Licensee shall be responsible for providing access to such records that in the ordinary course of business are in the possession or control of its Affiliates and Designees. Such examination shall be limited to a period of time no more than three (3) years immediately preceding the request for examination. The report of any such examination shall be made simultaneously to Genentech and Licensee and shall simply report the amount, if any, by which Licensee has overpaid or underpaid its royalties. If Licensee's royalties are found to be in error such that royalties to Genentech were underpaid, then Licensee shall promptly pay the deficiency

plus interest pursuant to Section 4.05 to Genentech; and if royalties to Genentech were underpaid by more than five percent (5.0%), then Licensee shall additionally reimburse Genentech for its reasonable costs incurred in examining such records.

4.02. *Reports*. Within sixty (60) days after the end of each Calendar Quarter following the First Commercial Sale of Licensed Product, Licensee shall furnish to Genentech a written report of all sales of all Licensed Product subject to royalty under Article III during such Calendar Quarter. Such report shall include, without limitation, (i) the determination of Net Sales as specified in Section 1.12, setting forth the amount of gross receipts, Net Sales, and any deduction taken from gross receipts to arrive at Net Sales, for each of Finished Product and Bulk Product separately; and (ii) the royalty payment then due. Concurrently with each report pursuant to this Section 4.02, Licensee shall make the royalty payment then due.

4.03. *Payments*. Payments shall be in United States dollars and, unless otherwise agreed in writing, shall be made by wire transfer of immediately available funds to such account of Genentech in such bank as Genentech may from time to time designate in writing. All royalty payments shall be free and clear of any taxes, duties, levies, fees or charges, except for withholding taxes. Licensee shall pay any withholding tax due on behalf Genentech and such withholding taxes shall be deducted from all payments due hereunder. The Parties shall cooperate to take advantage of the benefit of any double taxation treaty(ies) that may be applicable.

4.04. *Currency Conversion*. Royalties due on Net Sales of Licensed Product made in currency other than U.S. dollars shall be expressed in the currency of the invoice issued in connection with the sale of such Licensed Product together with the U.S. dollar equivalent of the royalty due, calculated

using the average rate of exchange published in Reuters during the applicable Calendar Quarter.

4.05. *Interest.* All royalty payments not made when due shall bear interest, calculated from the date such payment was due, at the annual rate of two percent (2%) over the prime rate of interest as reported in the *Wall Street Journal* on the day the payment was due.

## Article V

## REPRESENTATIONS, WARRANTIES, AND DISCLAIMERS

5.01. Genentech represents and warrants that it has the right to grant the license granted under this Agreement.

5.02. Nothing in this Agreement is or shall be construed as:

(i) A warranty or representation by Genentech as to the validity or scope of any claim or patent or patent application within the Licensed Patents;

(ii) A warranty or representation by Genentech that anything made, used, sold, or otherwise disposed of under any license granted in this Agreement is or will be free from infringement of any patent rights or other intellectual property right of any third party;

(iii) A grant by Genentech, whether by implication, estoppel, or otherwise, of any licenses or rights other than that expressly granted under Section 2.01; or

(iv) An obligation to bring or prosecute actions or suits against any third party for infringement of any of the Licensed Patents.

5.03. NO WARRANTY IS GIVEN WITH RESPECT TO THE LICENSED PATENTS, EXPRESS OR IMPLIED, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND THE PARTIES SPECIFICALLY DISCLAIM ANY EXPRESS OR IMPLIED WARRANTY OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY OF THE LICENSED PATENTS, OR NON-INFRINGEMENT OF THE PATENT OR OTHER RIGHTS OF ANY THIRD PARTY.

## Article VI

## LIABILITY

6.01. *Indemnification.* Licensee shall indemnify, defend and hold Genentech and its directors, officers, employees and agents harmless from and against any and all liabilities, claims, demands, expenses (including, without limitation, attorneys and professional fees and other costs of litigation), losses or causes of action in each of the foregoing cases of, by, for or to a third party (each, a "Liability") arising out of or relating in any way to (i) the possession, manufacture, use, sale or other disposition of Licensed Product by Licensee or its Affiliates or Designee hereunder, whether based on breach of warranty, negligence, product liability or otherwise, (ii) the exercise of any right granted to Licensee pursuant to this Agreement, or (iii) any breach of this Agreement by Licensee, except to the extent, in each case, that such Liability is caused by the gross negligence or willful misconduct of Genentech as determined by a court of competent jurisdiction; provided, however, that upon receiving notice of any such Liability, Genentech shall promptly notify Licensee and permit Licensee to handle and control the defense (including litigation and settlement) of such Liability, at Licensee's sole expense, and Genentech shall reasonably cooperate with the indemnifying Party in the defense of such Liability, at Licensee's sole expense. The indemnification of this Section 6.01 shall not apply to any settlement, compromise or ad-

mission of liability made by a person or entity to be indemnified hereunder without the written consent of Licensee.

## Article VII

## TERM AND TERMINATION

7.01. *Term*. The term of this Agreement will commence on the Effective Date and remain in full force and effect until the expiration of the last patent within the Licensed Patents (the "Term"), unless earlier terminated in accordance with this Article VII.

7.02 *Termination without Breach*. Licensee shall have the right to terminate this Agreement upon ninety (90) days prior written notice to Genentech.

7.03. *Termination for Breach*. Genentech shall have the right to terminate this Agreement and the licenses granted hereunder upon written notice to Licensee for a material breach of this Agreement if Licensee has failed to cure such breach within thirty (30) days following notice thereof. Licensee's failure to pay royalties and provide reports to Genentech under this Agreement when due shall constitute a material breach.

7.04. *Insolvency*. Genentech may terminate this Agreement if, at any time, Licensee shall file in any court pursuant to any statute of any individual state or country, a petition in bankruptcy, insolvency or for reorganization or for an agreement among creditors or for the appointment of a receiver or trustee of Licensee or of its assets, or if Licensee proposes a written agreement of composition or extension of its debts, or if Licensee shall be served with an involuntary petition against it filed in any insolvency proceeding, and such petition shall not be dismissed within sixty (60) days after the filing thereof, or if Licensee shall propose or be a party to any dissolution or liquidation, or if Licensee shall make an

assignment for the benefit of creditors. Any termination pursuant to this Section 7.04 shall be effective immediately upon notice of such termination.

7.05. *Effect of Termination.* Termination of this Agreement in whole or in part for any reason shall not relieve Licensee of its obligations to pay all fees and royalties that shall have accrued hereunder prior to the effective date of termination. Termination of this Agreement by or as to Licensee shall result in the termination of the licenses granted to Licensee and to all sublicensees of Licensee pursuant to this Agreement. The provisions of Article IV, Article V, Article VI, Article VIII and this Section 7.05 shall survive termination of the Agreement for any reason.

## Article VIII

## MISCELLANEOUS PROVISIONS

8.01. *Relationship of the Parties.* Nothing in this Agreement is intended or shall be deemed to constitute or give rise to a partnership, agency, distributorship, employer-employee, joint venture, or fiduciary relationship between the Parties. No Party shall incur any debts or make any commitments for the other.

8.02. *Patent Prosecution, Maintenance and Enforcement.* Genentech shall be solely responsible, at its sole discretion and expense, for the prosecution, defense, and maintenance of Licensed Patents, and for enforcing Licensed Patents against actual or suspected third party infringers.

8.03. *Assignment.* (a) Neither Party shall assign any of its rights or obligations hereunder except: (i) as incident to the merger, consolidation, reorganization or acquisition of stock or assets affecting substantially all of the assets or voting control of the assigning Party; (ii) to any corporation or other entity to which it may transfer substantially all of its assets related to the Licensed Product; (iii) to any wholly owned

subsidiary if the assigning Party remains liable and responsible for the performance and observance of all of the subsidiary's duties and obligations hereunder; or (iv) with the prior written consent of the other Party (which consent shall not be unreasonably withheld); provided however, that assignment in the context of insolvency or bankruptcy of Licensee shall require prior written consent of Genentech. This Agreement shall be binding upon the successors and permitted assigns of the Parties, and the name of a Party appearing herein shall be deemed to include the names of such Party's successor's and permitted assigns to the extent necessary to carry out the intent of this Agreement. Any assignment not in accordance with this Section 8.03 shall be void.

(b) Any assignment or transfer of rights by Genentech (in whole or in part) in or to Licensed Patents to any third party shall be subject to the grant of rights to Licensee herein.

8.04. *Further Acts and Instruments*. Upon request by either Party, the other Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be reasonably necessary or appropriate in order to carry out the purposes and intent of this Agreement.

8.05. *Trade Names and Trademarks*. Except as otherwise provided herein, no right, expressed or implied, is granted by this Agreement to use in any manner the name "Genentech" or any other trade name or trademark of Genentech in connection with the performance of this Agreement. Except as otherwise provided herein, no right, expressed or implied, is granted by this Agreement to use in any manner the name "MedImmune" or any other trade name or trademark of Licensee in connection with the performance of this Agreement.

8.06. *Entire Agreement*. This Agreement constitutes and contains the entire understanding and agreement of the Parties with respect to the subject matter hereof, and cancels and

supersedes any and all prior negotiations, correspondence, understandings and agreements, whether verbal or written, between the Parties respecting the subject matter hereof. No waiver, modification, or amendment of any provision of this Agreement shall be valid or effective unless made in writing and signed by a duly authorized representative of each of the Parties.

8.07. *Severability*. In the event any one or more of the provisions of this Agreement should for any reason be held by any court or authority having jurisdiction over this Agreement or either of the Parties to be invalid, illegal or unenforceable, such provision or provisions shall be validly reformed to as nearly as possible approximate the intent of the Parties and, if unreformable, shall be divisible and deleted in such jurisdiction; elsewhere, this Agreement shall not be affected so long as the Parties are still able to realize the principal benefits bargained for in this Agreement.

8.08. *Waiver*. The waiver by a Party of any breach of or default under any of the provisions of this Agreement or the failure of a Party to enforce any of the provisions of this Agreement or to exercise any right hereunder shall not constitute or be construed as a waiver of any other breach or default or as a waiver of any such rights or provisions hereunder.

8.09. *Choice of Law*. This Agreement shall be governed by and interpreted in accordance with the laws of the State of California without regard to conflict of laws provisions. This Agreement shall be construed as if drafted equally by the Parties, and in construing this Agreement no presumption shall operate in either Party's favor as a result of the role of it or its counsel in drafting or negotiating the terms or provisions hereof.

8.10. *Notices*. Any notice, request, consent, or other document required or permitted to be given under this Agreement or otherwise relating to this Agreement shall be in writing and

shall be deemed to have been sufficiently given if delivered in person, transmitted by facsimile (with a confirming copy sent by overnight courier), or sent by overnight courier or registered mail to the Party to whom it is directed at its address shown below or such other address as such Party shall have last given by notice to the other Party. Any such notice, requests, delivery, approval or consent shall be deemed received on the date of hand delivery or transmission by facsimile (provided that such date is a business day, otherwise it shall be deemed received on the next business day), one (1) business day after dispatch by overnight courier, or five (5) business days after dispatch of the registered mail.

*If to Licensee, addressed to*:

MedImmune, Inc.
35 West Watkins Mill Road
Gaithersburg, MD 20878
Attn: Manager, Business Development

Facsimile: (301) 527-4214

*If to Genentech, addressed to*:

Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080
Attn: Corporate Secretary

Facsimile: (650) 952-9881

8.11. *Confidentiality*. (a) Each Party shall be free to disclose the existence of this Agreement (but not its terms) to any third party. Neither Party shall disclose any of the terms (including, but not limited to, the financial terms) of this Agreement to any third party without the prior written consent of the other Party; provided, however, that each Party shall be free to disclose any of the terms of this Agreement (i) to the extent that a Party reasonably believes it is required to do so by securities or other applicable laws, regulations, or

rules (including the regulations or rules of any relevant stock exchange), (ii) pursuant to a legal proceeding or order of a court or governmental agency, (iii) to actual or prospective sublicensees, (iv) to City of Hope National Medical Center (in the case of Genentech), (v) to its accountants, attorneys and other professional advisors, or (vi) in connection with a financing, merger, consolidation, acquisition or a permitted assignment of this Agreement, provided that in the case of any disclosure under (iii), (iv), (v), or (vi) above, the recipient(s) are obligated and do so undertake to keep such terms of this Agreement confidential to the same extent as said Party, and provided that in the case of disclosure under (ii), the disclosing Party will use reasonable efforts to secure confidential treatment of such terms of this Agreement required to be disclosed.

(b) Genentech shall not disclose the content of reports of Section 4.02 and/or reports received under Section 4.01 other than to its accountants, attorneys and other professional advisors who are obligated to similar non-disclosure obligations, provided, however, that Genentech shall be free to disclose the content of reports of Section 4.02 and/or reports received under Section 4.01 (i) to the extent that Genentech reasonably believes it is required to do so by securities or other applicable laws, regulations, or rules (including the regulations or rules of any relevant stock exchange), (ii) pursuant to a legal proceeding or order of a court or governmental agency, (iii) to actual or prospective sublicensees, (iv) to City of Hope National Medical Center, (v) to its accountants, attorneys and other professional advisors, or (vi) in connection with a financing, merger, consolidation, acquisition or a permitted assignment of this Agreement, provided that in the case of any disclosure under (iii), (iv), (v), or (vi) above, recipient(s) are obligated and does so undertake to keep such content of reports of Section 4.02 and/or reports received under Section 4.01 confidential to the same extent as Genentech, and provided that in the case of

disclosure under (ii), Genentech will use reasonable efforts to secure confidential treatment of such content of reports of Section 4.02 and/or reports received under Section 4.01 required to be disclosed.

8.12. *Counterparts*. This Agreement may be executed simultaneously in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

8.13 *Bankruptcy*. All rights and licenses granted under or pursuant to this Agreement by Genentech to Licensee are, and shall irrevocably be deemed to be, "intellectual property" as defined in Section 101(56) of the U.S. Bankruptcy Code. In the event of the commencement of a case by or against either party under any Chapter of the above mentioned Bankruptcy Code, this Agreement shall be deemed an executory contract and all rights and obligations hereunder shall be determined in accordance with Section 365 of the above mentioned Bankruptcy Code, including, without limitation, Section 365(n) thereof.

IN WITNESS WHEREOF, Genentech and Licensee have caused this Agreement to be executed by their duly authorized representatives.

GENENTECH, INC.

By: Sean Johnston
Sean A. Johnston, Ph.D.
Title: Vice President, Intellectual Property

Date: January 28, 2003

MEDIMMUNE, INC.

By: David M. Mott
David M. Mott
Chief Executive Officer and Vice Chairman

Date: February 17, 2003

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

[Filed May 5, 2004]

---

Case No. CV03-2567 MRP (CTx)
Hon. Mariana R. Pfaelzer

---

MEDIMMUNE, INC.,

*Plaintiff,*

vs.

GENENTECH, INC., CITY OF HOPE, and CELLTECH R&D LTD.,

*Defendants.*

---

NOTICE OF APPEAL

Notice is hereby given that Plaintiff MedImmune, Inc. in the above named case hereby appeals to the United States Court of Appeals for the Federal Circuit from a Final Judgment dismissing MedImmune's First, Second, Third and Fourth causes of action as to both Genentech, Inc. and City of Hope, entered on April 30, 2004 (a copy of which is attached as Exhibit A). All claims as to all defendants in the above named action have now been dismissed.

Dated: May 5, 2004

DEWEY BALLANTINE LLP
By: /s/ Jeffrey R. Witham
JEFFREY R. WITHAM
Attorneys for Plaintiff
MEDIMMUNE, INC.

[Exhibit omitted in printing]

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

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04-1300, -1384

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MEDIMMUNE, INC.,
*Plaintiff-Appellant,*

v.

GENENTECH, INC.,
*Defendant-Appellee,*

and

CITY OF HOPE,
*Defendant-Appellee,*

and

CELLTECH, R&D, LTD.,
*Defendant-Appellee.*

---

JUDGMENT

ON APPEAL from the United States District Court for the Central District of California

In CASE NO(S). 03-CV-2567

This CAUSE having been heard and considered, it is

ORDERED and ADJUDGED: AFFIRMED

DATE: OCT. 18, 2005

ENTERED BY ORDER OF THE COURT
Vanxorbaly, Clerk

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

MEDIMMUNE V GENENTECH, 04-1300
DCT - 03-CV-2567

NOTICE OF ENTRY OF
JUDGMENT ACCOMPANIED BY OPINION

OPINION FILED AND JUDGMENT ENTERED:
10/18/05

The attached opinion announcing the judgment of the court in your case was filed and judgment was entered on the date indicated above. The mandate will be issued in due course.

Information is also provided about petitions for rehearing and petitions for rehearing en banc. The questions and answers are those frequently asked and answered by the Clerk's Office.

Costs are taxed against the Appellant(s) under Rule 39. The party entitled to costs is provided a bill of costs form and an instruction sheet with this notice.

The parties are encouraged to stipulate to the costs. A bill of costs will be presumed correct in the absence of a timely filed objection.

Costs are payable to the party awarded costs. If costs are awarded to the government, they should be paid to the Treasurer of the United States. Where costs are awarded against the government, payment should be made to the person(s) designated under the governing statutes, the court's orders, and the parties' written settlement agreements. In cases between private parties, payment should be made to counsel for the party awarded costs or, if the party is not represented by counsel, to the party pro se. Payment of costs should not be sent to the court. Costs should be paid promptly.

If the court also imposed monetary sanctions, they are payable to the opposing party unless the court's opinion provides otherwise. Sanctions should be paid in the same way as costs.

Regarding exhibits and visual aids: Your attention is directed to FRAP 34(g) which states that the clerk may destroy or dispose of the exhibits if counsel does not reclaim them within a reasonable time after the clerk gives notice to remove them. (The clerk deems a reasonable time to be 15 days from the date the final mandate is issued.

JAN HORBALY
Clerk

cc: HARVEY KURZWEIL
D. WALL, J. LIPNER, C. BARQUIST

SUPREME COURT OF THE UNITED STATES

---

No. 05-608

---

MEDIMMUNE, INC.,

Petitioner,

v.

GENENTECH, INC., et al.

---

ON PETITION FOR A WRIT OF CERTIORARI to the United States Court of Appeals for the Federal Circuit, No. 04-1300, 04-1384.

ON CONSIDERATION of the petition for a writ of certiorari herein to the United States Court of Appeals for the Federal Circuit.

IT IS ORDERED by this Court that the said petition is granted.

February 21, 2006

FILED
MAY 17 2006
OFFICE OF THE CLERK
SUPREME COURT, U.S.

No. 05-608

IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,
*Petitioner*,

v.

GENENTECH, INC., *et al.*,
*Respondents.*

**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## JOINT APPENDIX
## VOLUME II

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[Additional attorneys continued on inside cover]

* Counsel of Record

**PETITION FOR CERTIORARI FILED NOVEMBER 10, 2005**
**CERTIORARI GRANTED FEBRUARY 21, 2006**

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NOTICE

The following items have been omitted in printing this appendix because they appear in the following pages of the printed appendix to the petition for certiorari. They are incorporated herein by reference:

Amended memorandum of decision and order of the District Court (April 23, 2004) ..... 21a

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Certificates of service whenever appended to documents appearing herein have been omitted in printing. Some royalty numbers have been redacted; such redactions are noted by ellipses.

# United States Patent [19]

**Boss et al.**

[11] **Patent Number: 4,816,397**

[45] **Date of Patent: Mar. 28, 1989**


[54] **MULTICHAIN POLYPEPTIDES OR PROTEINS AND PROCESSES FOR THEIR PRODUCTION**


[75] Inventors: **Michael A. Boss**, Slough; **John H. Kenten**; **John S. Emtage**, both of High Wycombe; **Clive R. Wood**, Near Fordingbridge, all of United Kingdom

[73] Assignee: **Celltech, Limited**, Slough, United Kingdom



[21] Appl. No.: **672,265**

[22] PCT Filed: **Mar. 23, 1984**

[86] PCT No.: **PCT/GB84/00094**

§ 371 Date: **Nov. 14, 1984**

§ 102(e) Date: **Nov. 14, 1984**

[87] PCT Pub. No.: **WO84/03712**

PCT Pub. Date: **Sep. 27, 1984**

[30] **Foreign Application Priority Data**

Mar. 25, 1983 [GB] United Kingdom ..... 8308235

[51] **Int. Cl.**[4] ..... **C12P 21/00**; C12N 15/00; C12N 1/00; C12N 1/20

[52] **U.S. Cl.** ..... **435/68**; 435/172.3; 435/243; 435/255; 435/320; 435/252.31; 435/252.33

[58] **Field of Search** ..... 435/68, 172.3, 243, 435/320, 253, 255



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*Primary Examiner*—Blondel Hazel

*Attorney, Agent, or Firm*—Cushman, Darby & Cushman



[57] **ABSTRACT**

Multichain polypeptides or proteins and processes for their production in cells of host organisms which have been transformed by recombinant DNA techniques. According to a first aspect of the present invention, there is provided a process for producing a heterologous multichain polypeptide or protein in a single host cell, which comprises transforming the host cell with DNA sequences coding for each of the polypeptide chains and expressing said polypeptide chains in said transformed host cell. According to another aspect of the present invention there is provided as a product of recombinant DNA technology an Ig heavy or light chain or fragment thereof having an intact variable domain. The invention also provides a process for increasing the level of protein expression in a transformed host cell and vectors and transformed host cells for use in the processes.


**18 Claims, 13 Drawing Sheets**

U.S. Patent Mar. 28, 1989 Sheet 1 of 13 4,816,397

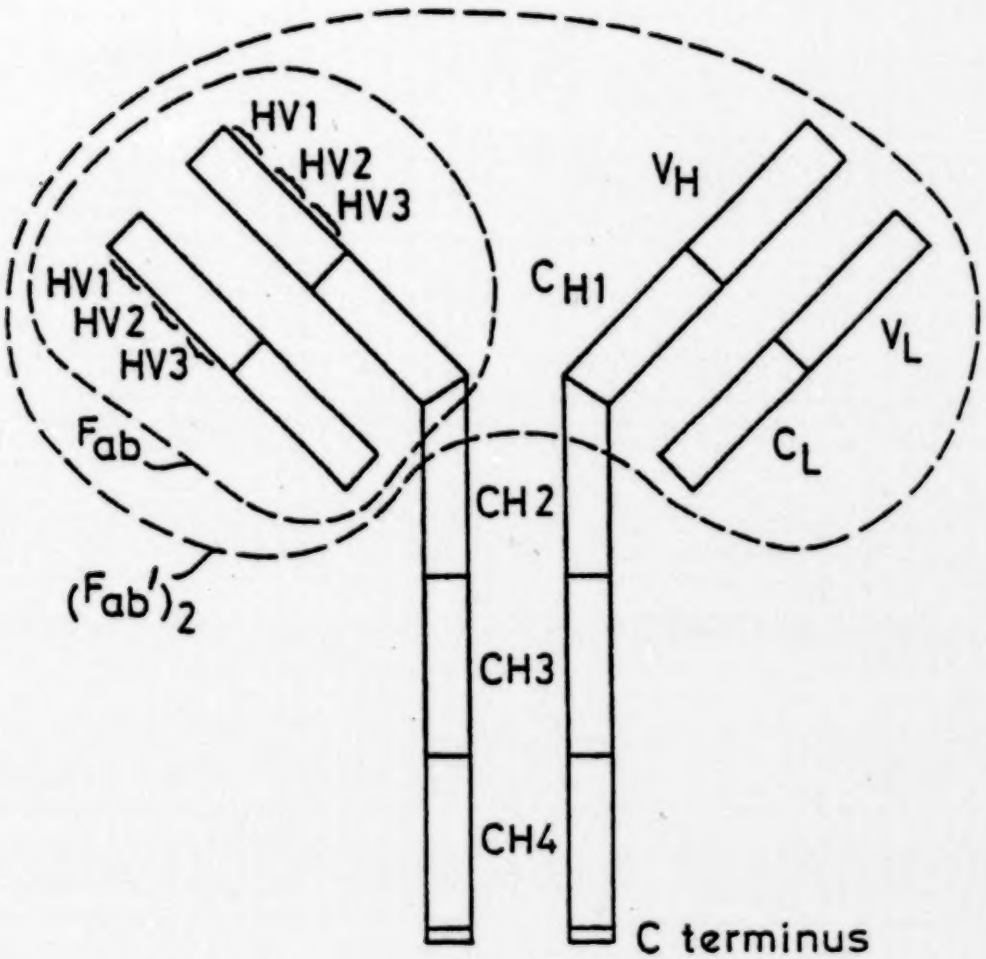
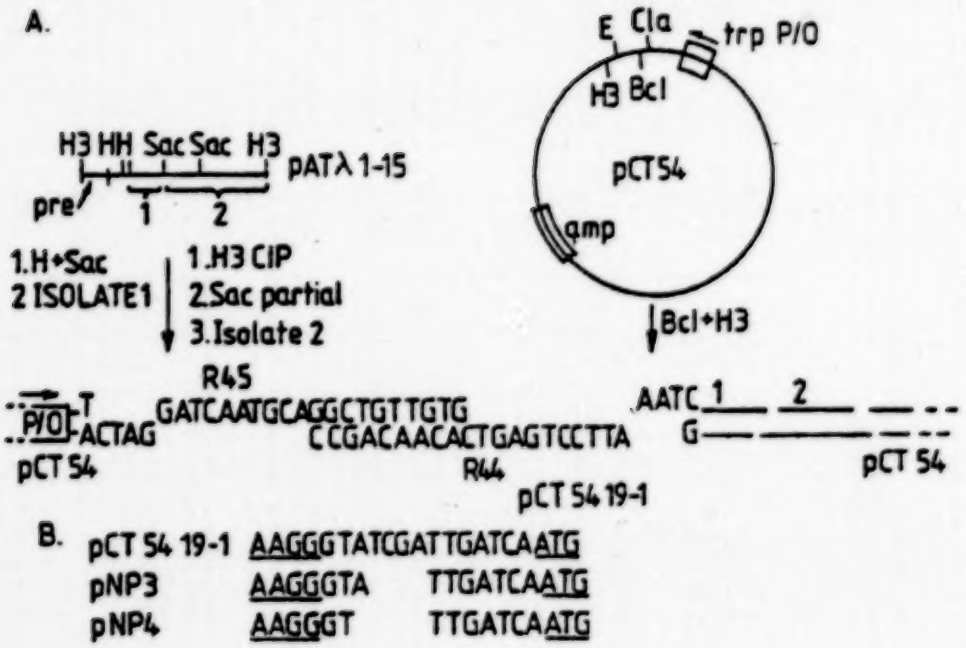



FIG. 1




B.

| | | |
|---|---|---|
| pCT 54 19-1 | AAGGGTATCGATTGATCAATG | |
| pNP3 | AAGGGTA | TTGATCAATG |
| pNP4 | AAGGGT | TTGATCAATG |

Legend. E = E corRI
H = HinfI
H3= Hind III

FIG. 2

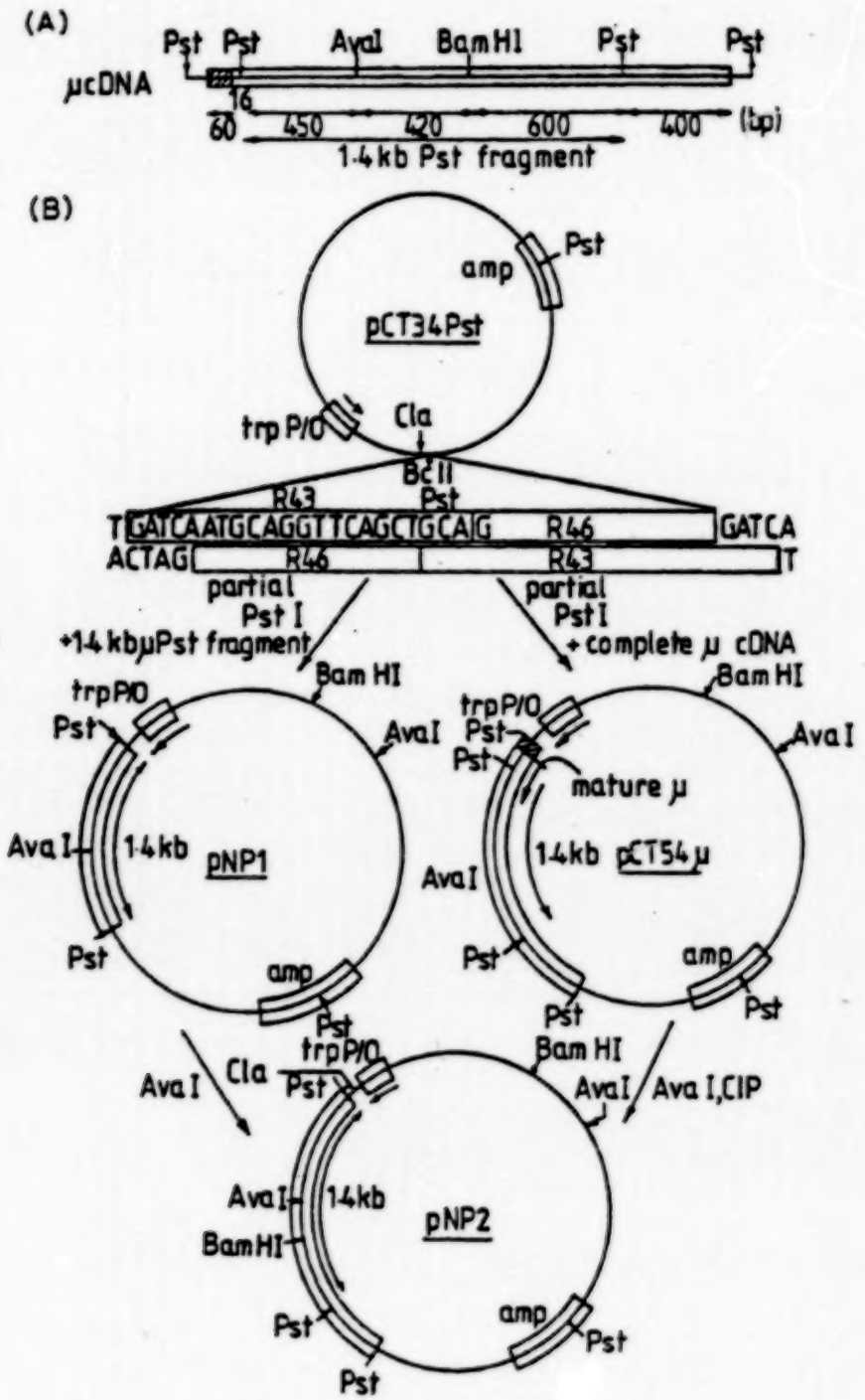

(A)
Pst Pst AvaI BamHI Pst Pst
μcDNA
16
60 450 420 600 400 (bp)
1.4kb Pst fragment
(B)
amp
Pst
pCT34Pst
trp P/O
Cla
BclI
Pst
R43
R46
GATCA
ACTAG
partial
Pst I
+1.4kbμPst fragment
+complete μ cDNA
Bam HI
trpP/O
Pst
AvaI
1.4kb
pNP1
mature μ
pCT54μ
Cla
AvaI, CIP
pNP2
BamHI

FIG. 3

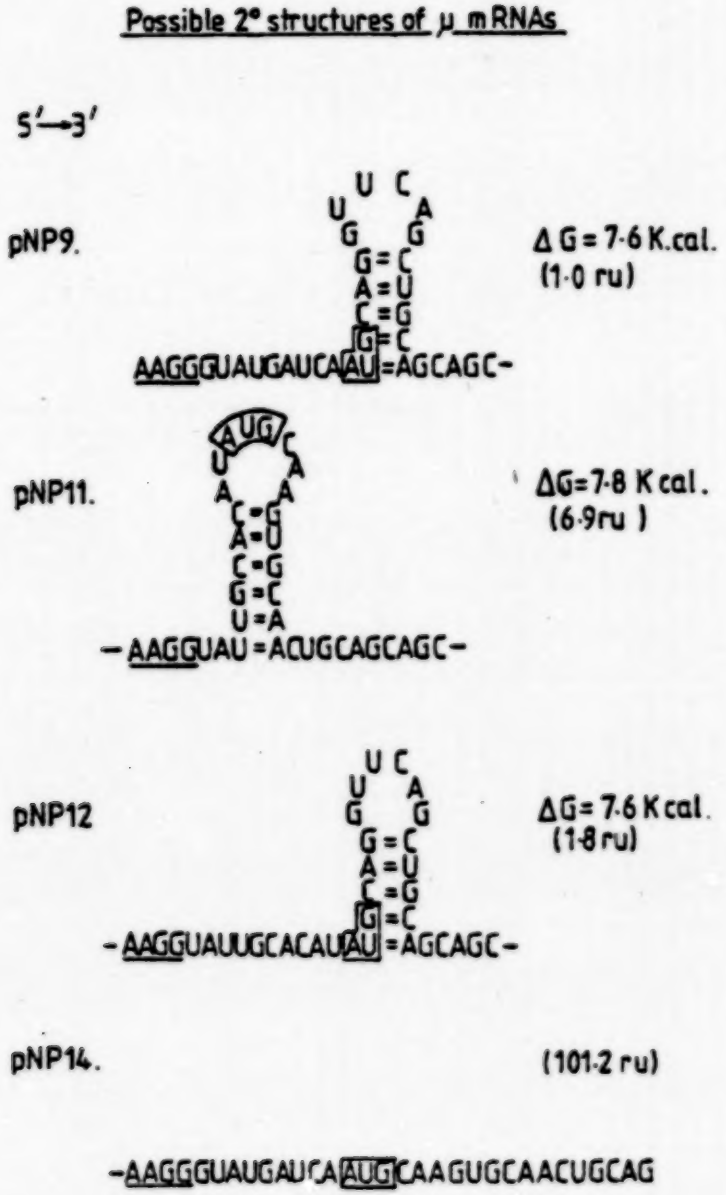

Possible 2° structures of μ mRNAs
5'→3'
pNP9.
ΔG = 7·6 K.cal.
(1·0 ru)
AAGGGUAUGAUCAAUG=AGCAGC-
pNP11.
ΔG=7·8 K cal.
(6·9ru )
-AAGGUAU=ACUGCAGCAGC-
pNP12
ΔG= 7·6 K cal.
(1·8 ru)
-AAGGUAUUGCACAUAUG=AGCAGC-
pNP14.
(101·2 ru)
-AAGGGUAUGAUCAAUGCAAGUGCAACUGCAG

FIG. 4

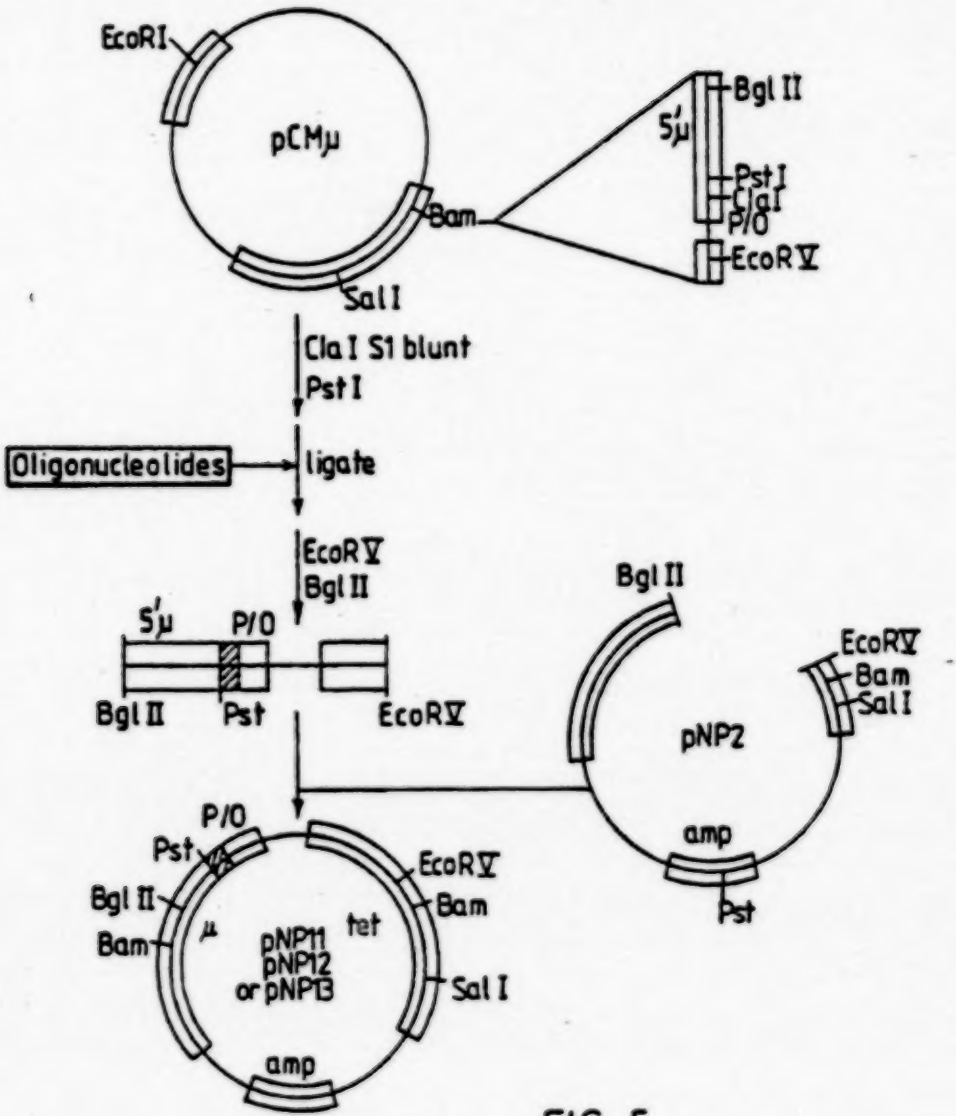

EcoRI
pCMμ
Bam
Sal I
5'μ
Bgl II
Pst I
Cla I
P/O
EcoR V
Cla I S1 blunt
Pst I
Oligonucleolides
ligate
EcoR V
Bgl II
5'μ
P/O
Bgl II
Pst
EcoR V
Bgl II
pNP2
EcoR V
Bam
Sal I
amp
Pst
P/O
Pst
Bgl II
Bam
μ
pNP11
pNP12
or pNP13
tet
EcoR V
Bam
Sal I
amp

FIG. 5

FIG. 6

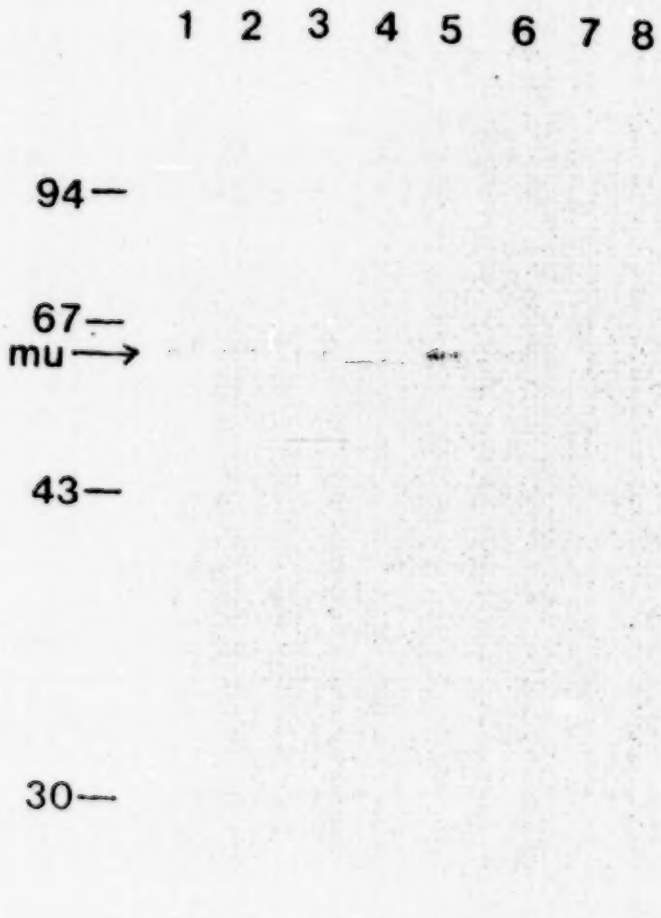



FIG. 7

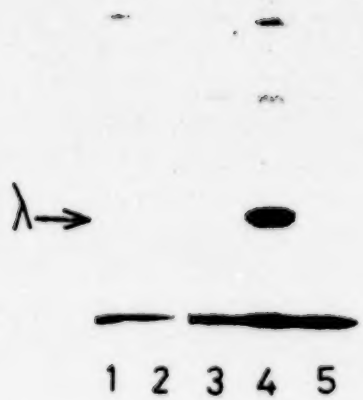



FIG. 8

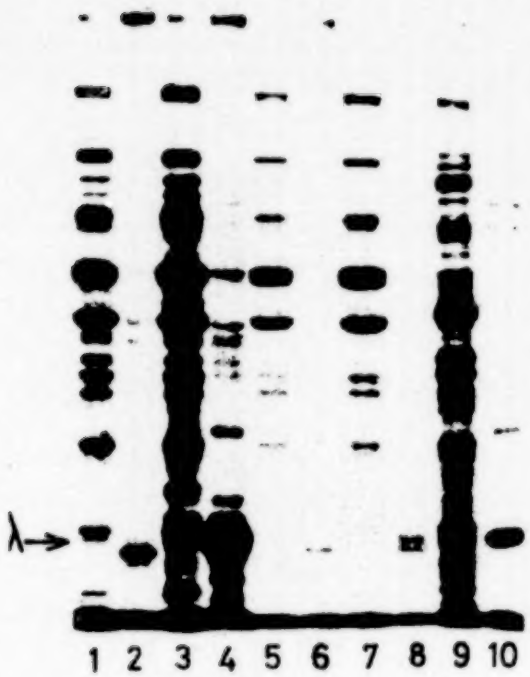



FIG. 9

FIG. 10

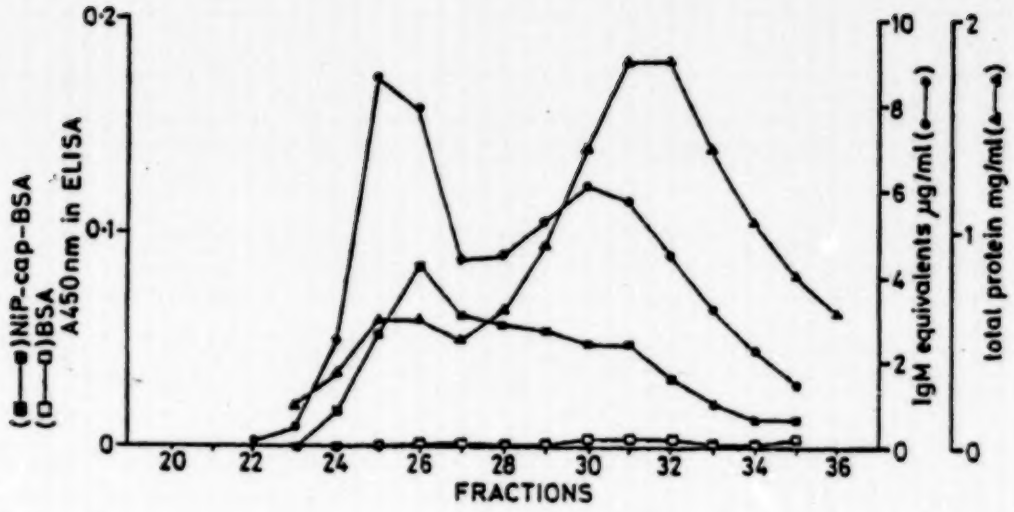

0·2
0·1
0
(■—■)NIP-cap-BSA
(□—□)BSA
A450nm in ELISA
10
8
6
4
2
0
IgM equivalents µg/ml (●—●)
2
1
0
total protein mg/ml (▲—▲)
20
22
24
26
28
30
32
34
36
FRACTIONS

FIG. 11

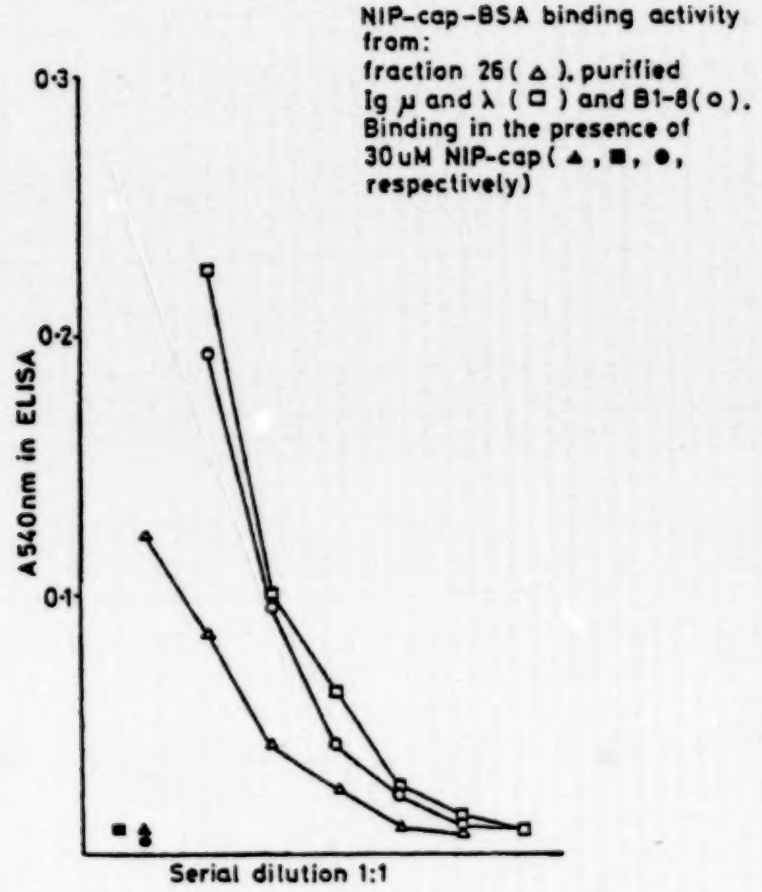
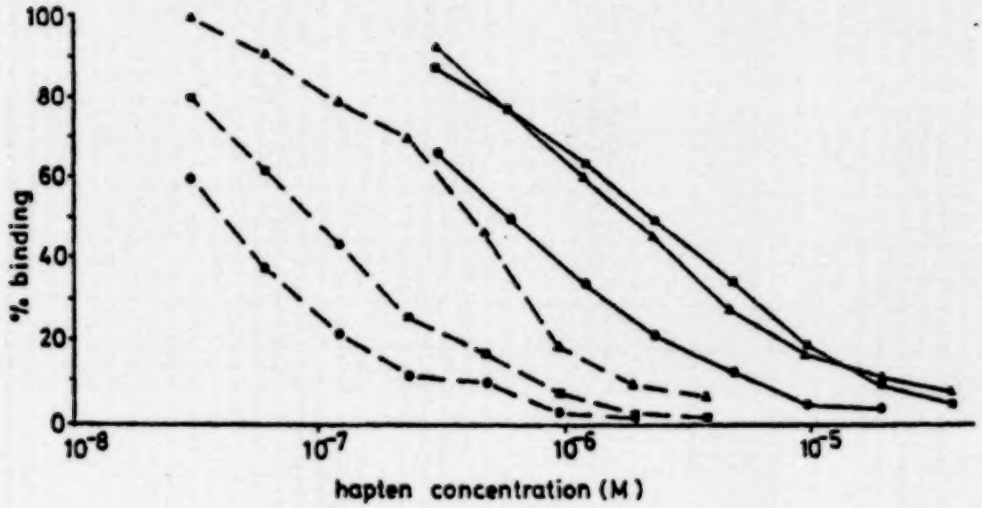

NIP-cap-BSA binding activity from:
fraction 26 ( △ ), purified Ig μ and λ ( □ ) and B1-8 ( ○ ).
Binding in the presence of 30 uM NIP-cap ( ▲ , ■ , ● , respectively)
0·3
0·2
0·1
A540nm in ELISA
Serial dilution 1:1

FIG. 12




Binding of antibodies to NIP-cap BSA B1-8 IgM (■), fraction 26 (▲), purified Ig μ or λ (●), in the presence of free NIP-cap (----) or NIP-cap (——).

FIG. 13

# MULTICHAIN POLYPEPTIDES OR PROTEINS AND PROCESSES FOR THEIR PRODUCTION

This invention relates to multichain polypeptides or proteins and processes for their production in cells of host organisms which have been transformed by recombinant DNA techniques.

In recent years advances in molecular biology based on recombinant DNA techniques have provided processes for the production of heterologous (foreign) polypeptides or proteins in host cells which have been transformed with heterologous DNA sequences which code for the production of these products.

Theoretically, the recombinant DNA approach may be applied to the production of any heterologous polypeptide or protein in a suitable host cell, provided that appropriate DNA coding sequences can be identified and used to transform the host cell. In practice, when the recombinant DNA approach was first applied to the production of commercially useful products, its application for the production of any specified polypeptide or protein presented particular problems and difficulties, and the success of applying this approach to the production of any particular polypeptide or product was not readily predictable.

However, a large number of heterologous single chain polypeptides or proteins have now been produced by host cells transformed by recombinant DNA techniques. Examples of such heterologous single chain polypeptides or proteins include human interferons, the A and B chains of human insulin, human and bovine growth hormone, somatostatin, calf prochymosin and urokinase. Such transformed host cells provide a reproducible supply of authentic heterologous polypeptiede or protein which may be produced on an industrial scale using industrial fermentation technology.

It should be pointed out that some of these polypeptides, for instance urokinase, after secretion by a host cell appear as two chain molecules. However, in such cases, the molecule is synthesised by the host cell as a single chain polypeptide, coded for by a single DNA sequence, which is cleaved in the host cell subsequent to synthesis to form the two chain structure.

It is known that in both human and animal systems there are a number of polypeptides or proteins which have multichain structure in which the chains are not derived from the cleavage of a single chain polypeptide coded for by a single DNA sequence. In such cases, the gene for each of the chains may be located at different points on the same chromosome or even on different chromosomes. In these cases, the polypeptide chains are synthesised separately and then assembled into the complete molecule subsequent to synthesis. Heretofore, no such multichain polypeptide or protein has been produced by recombinant DNA techniques from a single host cell.

A particular example of a class of such multichain polypeptides or proteins is the immunoglobulins.

Immunoglobulins, commonly referred to as antibodies, are protein molecules produced in animals by B-lymphocyte cells in response to challenge with foreign antigenic agents, such as bacteria, viruses and foreign proteins. The immunoglobulins comprise a crucial part of the immune systems of humans and animals. The immunoglobulins recognise specific parts of the foreign agents and bind onto them. The specific parts are usually known as antigenic determinants or antibody binding sites. A given foreign agent is likely to have a number of different antigenic determinants.

A typical immunoglobulin (Ig) molecule is shown in FIG. 1 of the accompanying drawings, to which reference is now made. The Ig molecule comprises two identical polypeptide chains of about 600 amino acid residues (usually referred to as the heavy chains H), disulphide bonded to each other, and two identical shorter polypeptide chains of about 220 amino acid residues (usually referred to as the light chains L), each light chain being disulphide bonded to one end of each heavy chain as shown.

When the Ig molecule is correctly folded, each chain is formed into a number of distinct globular areas, usually known as domains, joined by a more linear polypeptide chain. The light chains have two such domains, one of which is of variable sequence $V_L$, and the other of which is of constant sequence $C_L$. The heavy chains have a single variable domain $V_H$ adjacent the variable domain $V_L$ of the light chain, and three or four constant domains $C_{H1\text{-}3 \text{ or } 4}$.

The variable domains on both the heavy and the light chains each contain three hypervariable regions (HV1-3) which, when the Ig molecule is correctly folded, are located adjacent one another and form the antigen binding site. It is this area which recognises and binds to the antigenic determinant for which the Ig molecule is specific.

The constant domains of the Ig molecule do not take part in the binding to the antigenic determinant, but mediate the actions triggered by the binding of the Ig molecule to the antigenic determinant. It is believed that this triggering is caused by an allosteric effect induced by the binding of the Ig molecule to the antigenic determinant. The constant domain may enable the Ig molecule to fix complement or may cause mast cells to release histamine.

Ig's may be categorised by class or subclass, depending on which of a number of possible heavy chain constant domains they contain, there being eight such possible heavy chains in mice. Thus, for instance, and Ig molecule with a $\mu$ heavy chain belongs to the class IgM, and one with a $\gamma_1$ heavy chain to the class $IgG_1$.

Ig's may also contain one of two light chains, designated as $\kappa$ and $\lambda$ light chains, which have different constant domains and different sets of variable domains.

The structure of the Ig molecule and the location of the genes coding for the various domains thereof are discussed more fully by Early and Hood, in Genetic Engineering, Principles and Methods, Vol. 3, pages 153-158 (edited by Setlow and Hollaender, Plenum Press).

It is known that Ig molecules on digestion with selected enzymes can produce a number of immunologically functional fragments. Two such fragments are known as the $F_{ab}$ and $(F_{ab}')_2$ fragments. The $F_{ab}$ fragment comprises one light chain linked to the $V_H$ and $C_{H1}$ domains of a heavy chain as shown in FIG. 1. The $(F_{ab}')_2$ fragment consists essentially of two $F_{ab}$ fragments linked together by a small additional portion of the heavy chains as shown in FIG. 1. These fragments and other similar fragments can be of use in various tests and diagnostic and medical methods.

The principle method employed for the production of Ig's involves the immunisation of susceptible animals with the antigenic agent to provide an immune reaction. Generally the animal is immunised a second time to

improve the yield of Ig. The animal is then bled and the Ig is recovered from the serum.

However, the product of this method is not a homogeneous protein. The animal will produce Ig of different classes and also Ig specific for each of the different antigenic determinants on the antigenic agent, and its blood will therefore contain a heterogeneous mixture of Ig's. Obtaining a specific Ig of particular class and desired specificity from such a mixture requires very difficult and tedious purification procedures.

Recently, it has become possible to produce a homogeneous Ig of a single class and a single specificity by a technique first described by Kohler and Milstein (Nature, 256, 495–479, 1975). The technique involves the fusion of single Ig-producing parent cells with cancer cells to produce a monoclonal hybridoma cell which produces the Ig. Ig produced by this technique is usually known as monoclonal antibody. The nature of the monoclonal Ig is determined by the class and specificity of the Ig produced by the parent cell.

Recently attempts have been made to use recombinant DNA techniques to produce fragments of Ig molecules. For instance, Amster et al. (Nucleic Acid Research, 8, No. 9, 1980, pp 2055 to 2065) disclose the cloning of double stranded cDNA sequences encoding for a mouse Ig light chain into a plasmid. An E. Coli strain transformed by the plasmid synthesised a protein thought to comprise the complete constant domain of the light chain and about 40 amino acid residues of its variable region.

Kemp and Cowman (Proc. Natl. Acad. Sci. USA, 78, 1981 , pp 4520 to 4524) disclose the cloning of cDNA sequences encoding for mouse heavy chain fragments and the transforming of an E. Coli strain which then synthesised heavy chain polypeptide fragments.

In both these cases, the polypeptides were produced as fusion proteins, in which the fragments of the Ig polypeptides were fused with additional non-Ig polypeptide sequences, and the incomplete variable domains. Thus, the polypeptide chains produced in these studies were not immunologically functional polypeptides as they were incapable of combining with complementary heavy or light chains to provide Ig molecules having intact antigen binding sites and immunological function.

Research studies have also been carried out in mammalian systems. For instance, Falkner and Zachau (Nature, 298, 1982, pp 286 to 288) report the cloning of cDNA sequences encoding for mouse light chains into a plasmid which was used to transfect genomic eukaryotic cells which could then transiently synthesise light chains.

Rice and Baltimore (Proc. Natl. Acad. Sci. USA, 79, 1982, pp 7862 to 7865) report on the transfection of a functionally rearranged K light chain Ig gene into a murine leukemia virus-transformed lymphoid cell line. The cell line is then able to express the gene continuously. In both these cases, the K genes used to transfect the mammalian cells were obtained from myeloma cells and the K polypeptides produced were of indeterminate immunological function.

A further approach is exemplified in a series of papers by Valle et al. (Nature, 291, 1981, 338–340; Nature, 300, 1982, 71–74and J. Mol. Biol., 160, 1982, 459–474), which describe the microinjection of mRNAs encoding for heavy or light chains of Ig isolated from a mouse myeloma line into oocytes of Xenopus laevis. Under certain conditions complete Ig molecules were formed. However, the mRNAs were obtained from myeloma cells and the Ig molecules were of indeterminate immunological function.

It can thus be seen that hitherto it has not been possible to produce functional Ig by recombinant DNA technology.

According to a first aspect of the present invention, there is provided a process for producing a heterologous multichain polypeptide or protein in a single host cell, which comprises transforming the host cell with DNA sequences coding for each of the polypeptide chains and expressing said polypeptide chains in said transformed host cell.

According to a second aspect of the present invention, there is provided a heterologous multichain polypeptide or protein produced by recombinant DNA technology from a single host cell.

The present invention is of particular, but not exclusive, application in the production of Ig molecules and immunologically functional Ig fragments of the type referred to above. However, it will be appreciated that the present invention can be applied to the production of other multichain polypeptides or proteins.

In relation to the product of Ig molecules according to the invention it will be appreciated that, in order to produce a functional molecule, the DNA sequences used to transform the host cell will need to encode for at least the $V_L$ and $V_H$ domains of an Ig molecule. Moreover, these domains will need to be complementary so that when the two polypeptide chains fold together they form an antigen binding site of predetermined specificity.

Preferably, the Ig molecule or fragment include a complete light chain and at least the $C_{H1}$ domain in addition to the $V_H$ domain of the heavy chain. Most preferably the Ig molecule is intact.

It has also been shown by the present applicants that it is now possible to produce individual heavy and light chains having intact variable domains. This has not previously been possible. Therefore, according to a third aspect of the present invention there is provided as a product of recombinant DNA technology an Ig heavy or light chain or fragment thereof having an intact variable domain.

Advantageously, the Ig molecule or functional fragment thereof according to the present invention has a variable region (formed by the $V_L$ and $V_H$ domains) which defines a binding site for an antigenic determinant of clinical or industrial importance. The DNA coding sequences necessary to produce such a molecule may be derived from naturally occuring or hybridoma (monoclonal)Ig-producing cells with the desired specificity.

The constant domains of the Ig molecule or fragment, if present, may be derived from the same cell line as the variable region. However, the constant domains may be specifically altered, partially or completely omitted, or derived from a cell line producing a different class of Ig to provide Ig molecules or fragments having desired properties.

For example, an Ig molecule may be produced having variable domains ($V_H$ and $V_L$) idential with those from a monoclonal antibody having a desired specificity, and constant domain(s) from a different monoclonal antibody having desired properties, for instance to provide human compatibility or to provide a complement binding site.

Such alterations in the amino acid sequence of the constant domains may be achieved by suitable mutation or partial synthesis and replacement or partial or complete substitution of appropriate regions of the corresponding DNA coding sequences. Substitute constant domain portions may be obtained from compatible recombinant DNA sequences.

The invention may be utilised for the production of Ig molecules or fragments useful for immunopurification, immunoassays, cytochemical labelling and targetting methods, and methods of diagnosis or therapy. For example, the Ig molecule or fragment may bind to a therapeutically active protein such as interferon or a blood clotting factor, for example Factor VIII, and may therefore be used to produce an affinity chromatorgraphy medium for use in the immunopurification or assay of the protein.

It is also envisaged that the Ig molecule may be synthesised by a host cell with another peptide moiety attached to one of its constant domains. Such a further peptide moiety may be cytotoxic or enzymatic. Alternatively, the moiety may be useful in attaching the Ig molecule to a biological substrate, such a cell or tissue, or to a non-biological substrate, such as a chromatography medium. Such a peptide moiety is herein referred to as a structural peptide moiety.

It is further envisaged that cytotoxic, enzymic or structural peptide moieties could be attached to the Ig molecule by normal peptide chemical methods, as are already known in the art, rather than by being synthesised with the Ig molecule.

The Ig molecule or fragment may also comprise a therapeutic agent in its own right. For instance, an Ig molecule or fragment specific for D blood group antigen may be useful for the prevention of haemolytic disease of the new born.

Any suitable recombinant DNA technique may be used in the production of the multichain polypeptides or proteins of the present invention. Typical expression vectors such as plasmids are constructed comprising DNA sequences coding for each of the chains of the polypeptide or protein.

It will be appreciated that a single vector may be constructed which contains the DNA sequences coding for more than one of the chains. For instance, the DNA sequences coding for Ig heavy and light chains may be inserted at different positions on the same plasmid.

Alternatively, the DNA sequence coding for each chain may be inserted individually into a plasmid, thus producing a number of constructed plasmids, each coding for a particular chain. Preferably the plasmids into which the sequences are inserted are compatible.

The or each constructed plasmid is used to transform a host cell so that each host cell contains DNA sequences coding for each of the chains in the polypeptide or protein.

Suitable expression vectors which may be use for cloning in bacterial systems include plasmids, such as Col E1, pcR1, pBR322, pACYC 184 and RP4, phage DNA or derivatives of any of these.

For use in cloning in yeast systems, suitable expression vectors include plasmids based on a 2 micron origin.

Any plasmid containing an appropriate mammalian gene promoter sequence may be used for cloning in mammalian systems. Such vectors include plasmids derived from, for instance, pBR322, bovine papilloma virus, retroviruses, DNA viruses and vaccinia viruses.

Suitable host cells which may be used for expression of the heterologous multichain polypeptide or protein include bacteria, such as *E. coli* and *B. subtilis*, Streptomyces, yeasts, such as *S. cervisiae*, and eukaryotic cells, such as insect or mammalian cell lines. Examples of suitable bacterial host cells include *E. Coli* HB 101, *E. Coli* X1776, *E. Coli* X2882, *E. Coli* PS 410, *E. Coli* MRC 1, *E. Coli* RV308, *E. Coli* E103S and *E. Coli* B.

The present invention also includes constructed expression vectors and transformed host cells for use in producing the multichain polypeptides or proteins of the present invention.

After expression of the individual chains in the same host cell, they may be recovered to provide the complete multichain polypeptide or protein in active form, for instance to provide an Ig molecule of predetermined immunological function.

It is envisaged that in preferred forms of the invention, the individual chains will be processed by the host cell to form the complete polypeptide or protein which advantageously is secreted therefrom.

However, it may be that the individual chains may be produced in insoluble or membrane-bound form. It may therefore be necessary to solubilise the individual chains and allow the chains to refold in solution to form the active multichain polypeptide or protein. A suitable procedure for solubilising polypeptide chains expressed in insoluble or membrane-bound form is disclosed in our copending application No. (Protein Recovery, Agent's Ref. GF 402120 and 402121).

It will be appreciated that the present application shows for the first time that it is possible to transform a host cell so that it can express two or more separate polypeptides which may be assembled to form a complete multichain polypeptide or protein. There is no disclosure or suggestion of the present invention in the prior art, which relates solely to the production of a single chain heterologous polypeptide or protein from each host cell.

The present invention will now be described, by way of example only, with reference to the accompanying drawings, in which:

FIG. 1. shows a diagrammatic representation of a typical intact Ig molecule;

FIG. 2 shows the construction of plasmids for the direct synthesis of a λ light chain in *E. Coli;*

FIG. 3 shows the construction of plasmids for the direct synthesis of a μ heavy chain in *E. Coli;*

FIG. 4 is a diagrammatic representation of μ*m*RNA sequences around the initiation codon;

FIG. 5 shows the construction of plasmids having altered secondary structure around the initiation codon;

FIG. 6 is a polyacrylamide gel showing expression and distribution of μ protein from *E. Coli* B;

FIG. 7 is a polyacrylamide gel showing pulse chase autoradiograms of μ protein in *E. Coli* B and in *E. Coli* HB101;

FIG. 8 is a polyacrylamide gel showing the results of λ gene expression in *E. Coli;*

FIG. 9 is a polyacrylamide gel showing the distribution of recombinant λ light chain polypeptide between the soluble and insoluble cell fractions;

FIG. 10 is a polyacrylamide gel showing expression and distribution of λ protein from *E. Coli* E103S;

FIG. 11 shows the results of the fracitonation of μ and λ protein expressed by *E. Coli* B on DEAE Sephacel;

FIG. 12 shows the specific hapten binding of reconstituted Ig molecules; and

FIG. 13 shows the heteroclitic nature of the hapten binding of the reconstituted Ig molecules.

In the following examples, there is described the production of Ig light and heavy chain polypeptides derived from monoclonal antibodies which recognise and bind to the antigenic determinant 4-hydroxy-3-nitrophenyl acetyl (NP), using *E. coli* and *S. cerevisiae* as the host cells Recombinant DNA techniques were used to enable the host cells to express both the polypeptide chains.

It will be appreciated that the invention is not limited to the specific methods and construction described hereafter.

## Construction of Lambda Light Chain Expression Plasmid

FIG. 2, to which reference is now made, shows schematically the method used to construct a λ light chain expression plasmid.

It was decided to express the lambda gene in *E. coli* by direct expression of the gene lacking the eucaryotic signal peptide but containing a methionine initiator residue at the amino-terminus (met-lambda). The approach used for bacterial synthesis of met-lambda was to reconstruct the gene in vitro from restriction fragments of a cDNA clone and to utilise synthetic DNA fragments for insertion into the bacterial plasmid pCT54 (Emtage et al., proc. Natl. Acad. Sci. USA., 80, 3671 to 3675, 1983). This vector contains the *E. coli* trp promoter, operator and leader ribosome binding site; in addition 14 nucleotides downstream of the ribosome binding site is an initiator ATG followed immediately by $EcoR_I$ and HindIII sites and the terminator for *E. coli* RNA polymerase from bacteriophage T7.

As a source of light chain we used a plasmid pABλ-1-15 which contains a full-length $\lambda_1$ light chain cDNA cloned into the PstI site of pBR322. This $\lambda_1$ light chain is derived from a monoclonal antibody, designated S43, which binds to 4-hydroxy-3-nitrophenylacetyl (NP) haptens.

In order to create a HindIII site 3' to the end of the lambda gene for insertion into the HindIII site of pCT54, the cDNA was excised from pAB λ 1-15 using PstI. The cohesive ends were blunt ended using the Klenow fragment of DNA polymerase and synthetic HindIII linker molecules of sequence 5'-CCAAGCTTGG-3' ligated. The DNA was digested with HindIII and the 850bp lambda gene isolated by gel electrophoresis and cloned into HindIII cut pAT153 to yield plasmid pAT λ 1-15. The 3' end of the lambda gene was isolated from pAT λ 1-15 by HindIII plus partial SacI digestion as a 630bp SacI-HindIII fragment (2 in FIG. 2). The HindIII cohesive end was dephosphorylated by calf intestinal alkaline phosphatase during isolation of the fragment to prevent unwanted ligations at this end in subsequent reactions.

A HinfI restriction site is located between codons 7 and 8 and the lambda sequence. The 5' end of the lambda gene was isolated as a 148bp HinfI to sacI fragment (1 in FIG. 2).

Two oligodeoxyribonucleotides were designed to restore condons 1-8, and to provide an initiator ATG as well as BclI and HinfI sticky ends. The two chemically synthesised oligonucleotides made to facilitate assembly of the gene had the sequences:

R45 5'-pGATCAATGCAGGCTGTTGTG 3'

R44 3' CCGACAACACTGAGTCCTTAp- 5'

pCT54 was cut with both BclI and HindIII and the resulting linear molecules isolated, mixed together with the two oligodeoxyribonucleotide linkers R44 and R45 and both fragments 1 and 2, and ligated using T4 ligase (FIG. 2). The mixture was used to transform *E. coli* DH1 to ampicillin resistance. Recombinant clones in pCT54 were identified by hybridisation of DNA from replica plated colonies on nitrocellulose to a nick-translated probe derived from the pAT λ 1-15 insert.

A clone was identified which hybridised to lambda cDNA and also showed the predicted restriction fragment pattern. This plasmid (designated pCT54 19-1) was sequenced from the ClaI site and shown to have the anticipated sequence except that there was a mutation of the fourth codon from CTG to ATG, changing the amino acid at this point from valine the methionine.

The sequence in this area was:

```
... GATTGATCA.ATG.CAG.GCT.GTT.ATG.ACT.CAG.GAA.TCT.GCA.CTC.ACC.ACA.TCA
      met  gln  ala  val  met  thr  gln  glu  ser  ala  leu  thr  thr  ser
```

The restriction enzyme sites in pCT54 between the Shine and Dalgarno sequence (AAGG), which is important for ribosome binding, and the ATG allow for the adjustment of the SD-ATG distance, an important parameter in determining expression rates. The SD-ATG distance was reduced by cutting the plasmid with ClaI or BclI and creating blunt ended species by digestion with $S_1$ nuclease. 2 μg of ClaI cut DNA was digested with 200 units of $S_1$ nuclease for 30 minutes at 30° using standard buffer conditions. The solution was deproteinised with phenol and the DNA recovered by ethanol precipitation. This DNA on religation with T4 DNA ligase and transformation into *E. coli* strain HB101 gave rise to a number of plasmids which had lost the ClaI or BclI site.

The plasmids which had lost their ClaI site were sequenced in the region surrounding the initiator ATG.

```
... AAGGGTATTGATCAATG CAG ... plasmid pNP3
      SD                met  glu

... AAGGGTTTGATCAATG CAG      plasmid pNP4
      SD                met  glu
```

In order to achieve high level expression a number of other approaches were followed. Firstly, a series of constructs were obtained which had increasing amounts of the 3' untranslated region of the cDNA removed by Bal 31 exonuclease. Secondly, a high copy number plasmid containing λcDNA was constructed. This plasmid contained a par function (Meacock, P. A. and Cohen, S. N., Cell, 20, 529-542, 1980) as well as being present in high copy number. Thirdly, the pNP3 plasmid was transformed into a number of protease-deficient strains or into HB101 in conjunction with a protease deficient dominant acting plasmid (Grossman, A. D. et al, Cell, 32, 151-159, 1983).

Construction of μ Heavy Chain Expression Plasmid

The full-length μ heavy chain cDNA derived from the NP binding monoclonal antibody B1-8 had been cloned into the PstI site of pBR322 yielding a plasmid designated pABμ-11 (Bothwell et al, Cell, 24, 625-637, 1981). In order to achieve high level expression, the μ cDNA minus the eukaryotic leader was reconstructed into pCT54. The construction of the μ heavy chain expression plasmid is shown diagramatically in FIG. 3. Two chemically synthesised oligonucleotides were made to facilitate this. These have the following sequences:

R43 5' GATCAATGCAGGTTCAGCTGCA 3'

R46 3' TTACGTCCAAGTCG 5'

These were ligated into BclI cut pCT54 using T4 DNA ligase and the resulting plasmid designated pCT54 Pst. The linkers were designed to replace the sequence in pCT54 between the BclI site and the ATG, to provide an internal PstI site and to recreate the sequence from pABμ-11 5' to the PstI site up to codon +1. pCT54 Pst was cut briefly was PstI, treated with alkaline phosphatase and full length DNA glass isolated from a 1% agarose gel. Similarly pABμ-11 was briefly cut with PstI and the full length μ insert isolated following agarose gel electrophoresis. The μ cDNA was ligated with the full length pCT54Pst fragment using T4 DNA ligase under standard conditions and a plasmid designated pCT54μ was identified which by restriction enzyme analysis was shown in contain a full-length μ insert. The plasmid was sequenced around the 5' linker region and was found to have the anticipated sequence:

5' . . .
TGATCAATGCAGGTTCAGCT-
GCAGGGGGGGGATGGATGGAG . . . 3',

demonstrating that it was, indeed, a full length clone. A complete PstI digest of pCT54μ liberated a 1.4 Kb fragment which was purified by 0.8% agrose gel electrophoresis and glass powder isolation. This was ligated with PstI cut pCT54 Pst (see above) using T4 DNA ligase under standard conditions, followed by transformation into HB101. A plasmid designated pNP1 was isolated which was shown by restriction endonuclease pattern analysis to contain the 1.4 Kb μcDNA fragment in an appropriate orientation (FIG. 3). pNP1 was a plasmid which consisted of an appropriate 5' end for expression, whilst pCT54 contained an appropriate 3' end. The full length gene was reconstructed into pCT54 by cutting both pNP1 and PCT54μ with AvaI which cuts once in the plasmid and once in the μ gene. Both digests were run on a 1% agrose gel and the 1.9 kb fragment from pNP1 and the 3.65 kb fragment from pCT54μ isolated. Following alkaline phosphatase treatment of the 3.65 pCT54μ fragment, the two pieces of DNA were ligated to each other and transformed into HB101. A plasmid designated pNP2 was identified which demonstrated the correct restriction endonuclease pattern. It was sequenced in the area surrounding the initiator ATG and found to have the anticipated sequence:

5' . . .
TTGATCAATGCAGGTTCAGCTGCAG-
CAGCCTGGGGCTGAGCTTGTGAAG . . . 3'

The vector pCT54 had been constructed to include two restriction sites (BclI and ClaI) between the S-D sequence (AAGG) and the initiation codon so that the distance between these sequence elements could be varied. As most *E. coli* mRNAs have 6-11 nucleotides between the S-D sequence and the AUG, the distance in pNP2 was reduced by modification at the ClaI site. pNP2 was cut with ClaI and incubated with S1. The amount of S1 nuclease was adjusted so that some DNA molecules would lose 1-2 extra base pairs as a result of 'nibbling' by the enzyme. This DNA on religation with T4 DNA ligase and transformation into *E. coli* strain HB101 gave rise to a number of colonies harbouring plasmids which had lost the ClaI site. The sequences around the initiation codon of four plasmids pNP223, pNP261, pNP9 and pNP282 were determined and are given in Table 1, part A below.

TABLE 1

| | | S—D to ATG distance (no. of residues) | Sequence (5' - 3') Clot | Expression:(mu)(ru) expts. A | B | C |
|---|---|---|---|---|---|---|
| (A) | pNP2 | 14 | —AAAAAGGGTATCGATTGATCA[ATG]CAGGTTCAG— | 0.7 | 0.6 | 0.8 |
| S1 derivatives of pNP2 | pNP223 | 12 | —AAAAAGGGTATATTGATCA[ATG]CAGGTTCAG— | — | 0.7 | 0.6 |
| | pNP261 | 10 | —AAAAAGGGTATTGATCA[ATG]CAGGTTCAG— | — | 1.1 | 1.1 |
| | pNP282 | 7 | —AAAAAGGGTGATCA[ATG]CAGGTTCAG— | — | 0.7 | 0.6 |
| | pNP9 | 9 | —AAAAAGGGTATGATCA[ATG]CAGGTTCAG— | 1.0 | 1.0 | 1.0 |
| (B) | pNP11 | 11 | —AAAAAGGGTATTGCACAT[ATG]CAAGTGCAA— | 5.3 | 6.3 | 9.1 |
| oligo constructs | pNP12 | 11 | —AAAAAGGGTATTGCACA[ATG]CAGGTTCAG— | 1.8 | 2.3 | 1.3 |

TABLE 1-continued

| | S—D to ATG distance (no. of residues) | Sequence (5' - 3') Clot | Expression:(mu)(ru) expts. A | B | C |
|---|---|---|---|---|---|
| pNP14 | 9 | —AAAAAGGGTATGATCA[ATG]CAAGTGCAA— | 72.2 | 106.7 | 124.6 |
| pNP8 | — | — | 77.0 | 53.4 | 145.5 |
| pCT70 | — | — | 0 | 0 | 0 |

The expression of these constructs in *E. coli* B was examined in three experiments, and concentrations of μ protein were determined by ELISA as relative units (ru), a measure of μ concentration normalised to pNP9. The results are shown in Table 1.

Inductions were carried out by resuspending cells at 1:50 dilution from overnight cultures into induction medium, consisting of: $KH_2PO_4$ (3 g/l), $Na_2HPO_4$ (6 g/l), NaCl (0.5 g/l), Difco vitamin assay casamino acids (30 g/l), $NH_4Cl$ (4 g/l), glycerol (16 g/l), proline (0.5 g/l), Difco yeast extract (1 g/l), $CaCl_2.6H_2O$ (0.022 g/l), $MgSO_4.7H_2O$ (0.025 g/l), thiamine (0.01 g/l) and carbenicillin (0.1 g/l). Cultures were shaken at 37° C. and cells harvested by centrifugation.

ELISA assays were performed essentially as described by Patel et al. (Nucleic Acid Research, 10, 5605 to 5620, 1982), using affinity purified goat anti-mouse IgM (Tago) and affinity purified goat anti-mouse IgM (Tago) conjugated peroxidase, with 3,3',5,5' tetramethylbenzidine (Miles) as a substrate. Bacterial cell pellets were boiled for 2 minutes in 9M urea (BRL) and loaded directly into the ELISA, such that all wells contained 2.25M urea, 10 mM Tris-HCl pH 7.8 150 mM NaCl, 0.05% NP40 and 0.5% casein (Hammarsten, B. D. H.).

Altering the S-D to ATG distance with nuclease S1 was found to increase the level of μ expression, relative, to the parental plasmid pNP2, but only to a small extent (compare pNP9). The optimal S-G to AUG distance was found to be 9–10 nucleotides, as found in pNP9 and pNP261 respectively.

### Secondary Structure Analysis

Hairpin loops were identified by use of the computer programme HAIRGU developed by Dr. Roger Staden. The ΔG values were calculated as described by Trioco et al. (Nature NB, 246, 40–41, 1973).

Analysis of the potential secondary structure of μ mRNA encoded by pNP2 and pNP9 (one of the S1 derivatives of pNP2) revealed an extensive array of possible hairpin loops. Attention was focused on the region of this mRNA containing the ribosome binding site since the sequestering of S-D sequences and initiation codons into secondary structure may inhibit the initiation of translation. It was found that a hairpin loop including the U and G of the initiation codon could be formed (see FIG. 4). This hairpin loop is formed entirely within coding sequences and has a $\Delta G = -7.6$ kcal. No secondary structures were found which buried the S-D sequence, and none which mutually excluded the hairpin loop described above, and which had a lower ΔG.

To test whether expression of μ protein could be influenced by changes designed to alter potential secondary structure in the ribosome binding region, we used synthetic oligonucleotides to mutagenise this region of μ mRNA. The plasmids were constructed by insertion of a pair of oligonucleotides between the blunted Cla I site and the 5' Pst site of μ in pNP2 (see FIG. 5). The cloning strategy used to accomplish this, however, was multi-staged due to the presence of four Pst sites in pNP2. The vector pACYC184CM, which lacks Cla I and Pst I sites, was first constructed by cutting pACYC184 at its unique Cla I site, 'filling-in' the cohesive termini using T4 DNA polymerase and religating. Next, PACYC184CM was cut with BamHI, and the BamHI fragment from pNP2, bearing the 5'μ sequence, was inserted into it to form pCMμ (see FIG. 4). The vector pCMμ contained unique Cla I and Pst sites which were required for the oligonucleotide cloning (see FIG. 5).

pcMμ was cut with Cla I to completion, blunted with nuclease S1, and then cut with Pst I. The cut plasmid was purified by agarose gel electrophoresis and ligated separately with pairs of oligonucleotides, with the latter in a 100-fold molar excess. The pairs of oligonucleotides used were: R131 and R132 (for pNP11); R196 and R197 (for pNP12); and R202 and R203 (for pNP14). These have the sequences given below.

TGCACATATGCAAGTGCAACTGCA (R131),

GTTGCACTTGCATATGTGCA (R132),

GCTGAACCTGCATATGTGCA (R196),

TGCACATATGCAGGTTCAGCTGCA (R197),

GTTGCACTTGCATTGATC (R202),

GATCAATGCAAGTGCAACTGCA (R203).

The ligation mixture was then used to transform HB101. Recombinant clones were detected by colony hybridisation, on nitrocellulose filters, using one of each pair of oligonucleotides as a probe. Positive clones were sequenced and shown to have the correct nucleotide sequence. The μ sequences containing the cloned oligonucleotides were excised on Eco RV-Bgl II fragments. These were ligated to Eco RV-Bgl II cut pNP2 to reconstruct the full length μ genes (see FIG. 5). Three different plasmids were created by these procedures; pNP11, pNP12 and pNP14, having the nucleotide sequences shown in Table 1 above.

In the construct pNP11 the potentially deleterious hairpin loop of pNP2 was abolished by changing the residues in the degenerate position of three codons and by introducing a different S-D to AUG sequence. These changes allow the region between the S-D and AUG to base pair with the 5' end of μ coding sequence to form a hairpin loop of $\Delta G = -7.8$ kcal, approximately equal to that of pNP2, but leaving the AUG and S-D sequences exposed (see FIG. 4). The only other mutually exclusive hairpin loops are of $\Delta G = -2.3$, $-3.6$ and $+0.4$ kcal.

The construct pNP12 retains the S-D to AUG sequence of pNP11, but has the coding sequence of pNP2, such that the hairpin loop of pNP2 can form (see FIG. 4).

The final μ construct was pNP14, which had the S-D to AUG sequence of pNP9, but the 5' coding sequence of pNP11, so that the hairpin loop of pNP12 could not form. The construct pNB14 had no secondary structure burying the S-D or μ AUG.

### μ Protein Expression from Constructs with Differing mRNA Secondary Structures

*E. coli* B strains containing plasmids pNP9, pNP11, pNP12 and pNP14 were grown in induction medium and samples removed for ELISA assay. The concentration of μ was increased 6–7 fold in *E. coli* B cells containing pNP11 relative to pNP9 (see Table 1, Part b). Plasmid pNP12, which has the S-D to AUG sequence of pNP11, but the coding sequence of pNP9, showed only a two-fold increase in level of μ expression compared to pNP9.

Plasmid pNP14, which has the S-D to AUG sequence of pNP9 but the 5'μcoding sequence of pNP11, and thus differed from pNP9 only in three residues, was found to express μ protein over 90 times that found in pNP9.

A plasmid, pNP8, has also been constructed, from which μ is expressed, also from the trp promoter, as part of a trpE-μ fusion protein containing the amino terminal 53 amino acids of trpE and the carboxyl terminal 503 amino acids of μ. The rationale for making this fusion gene was that μ would be translated from an effective bacterial ribosome binding site rather than from one of unknown efficiency. Then, by comparing the amounts of trpE-μ produced from pNP8 with those of μ produced from the different constructs, an estimate of relative ribosome binding efficiency may be made. When the trpE-μ gene in pNP8 was induced and the products quantitated by ELISA, it was found that the μ expression in strains containing pNP8 and pNP14 was very similar (see Table 1, part B). The ribosome binding site (RBS) sequences of pNP11, pNP12 and pNP14 were designed in order to test the hypothesis that sequestering of the initiation codon into secondary structure inhibits translation initiation, and to increase the rate of initiation by releasing the initiation codon. In pNP11, the RBS hairpin loop of pNP2 and pNP9 was abolished by changing the 5'μcoding sequence in the degenerate position of three codons. In addition, the S-D to AUG sequence was changed to allow the base-pairing of this region with the 5' coding sequence. The result of these changes is that the initiation codon is exposed in the loop of a hairpin with the S-D sequence at the base of the stem (see FIG. 4). This hairpin loop had a ΔG approximately equivalent to the ΔG of the pNP9 hairpin loop. Strains containing pNP11 produced 6–7 times as much μ as did those with pNP9. To test whether this was due to the change in S-D to ATG sequence characteristics, rather than to the liberation of the initiation codon, pNP12 was constructed as a control. The latter has the S-D to AUG sequence of pNP11, but retains the 5'μ coding sequence of pNP9, so that the RBS hairpin loop of pNP11 cannot form, but the potentially deleterious one of pNP9 can form. The level of μ expression from pNP12 was found to be increased by only two-fold relative to pNP9. This increase is probably due to an altered S-D to AUG distance, a U immediately 5' to the initiation codon, and the S-D to AUG sequence being G-poor each of which has been shown to be advantageous. It is therefore likely that the increased expression from pNP11 is due to a preferable mRNA secondary structure. The RBS hairpin loop of pNP9 probably acts to inhibit translation while creation of another hairpin loop which exposes the initiation codon is responsible for the increased expression.

The plasmid pNP14 was constructed, such that it had the S-D to AUG sequence of pNP9, but the coding sequence of pNP11. The expression plasmid pNP14, therefore, differed from pNP9 in only three residues, those in the degenerate position of three codons, yet strains containing pNP14 expressed over ninety times more μ than those containing pNP9. This increase in expression cannot be explained on the basis of the three residue changes optimizing codon usage, for they introduce less favoured codons, as judged by the frequency of their occurrence in strongly expressed *E. coli* genes.

The increased expression is best explained by the abolition of the RBS hairpin loop in pNP9. The magnitude of the increases in expression observed, and the few residue changes introduced, makes it difficult for these results to be interpreted in terms of changes in mRNA stability.

The expression of pNP8, which encodes the trpE-μ fusion protein from a native trpE RBS, was also examined, and found to express at approximately the same level as pNP14. This may indicate that the RBS of pNP14 is equivalent to that of trpE in terms of its efficiency in directing translation initiation. The native trpE RBS of pNP8 and that of pNP14 were found to have no secondary structures hindering the use of their RBS sequences.

### Expression of μ Protein in *E. Coli*

*E. Coli* B cells containing the μ expression plasmid pNP11 were grown under inducing conditions and soluble and insoluble extracts prepared, and analysed by SDS-PAGE. A novel band was seen after staining the gel with Coomassie blue in the lane containing proteins from the insoluble fraction (see FIG. 6, lane 2). This band was not seen in the negative control lane which contained proteins from the same fraction from cells harbouring pCT70 (see FIG. 6, lane 3). The novel band was found to migrate to a position corresponding to a protein of a molecular weight within less than 5% of the actual molecular weight of non-glycosylated μ of 62.5 Kd. A duplicate set of lanes were transferred to nitrocellulose, and Western blotted. Alignment of the stained gel and the blot autoradiogram confirms that this novel band is antigenically related to IgM (see FIG. 6, lanes 4 and 8). No band was found in extracts from cells containing pCT70 (see FIG. 6, lanes 5 and 7). Only a low amount of μ was found in the soluble fraction (see FIG. 6, lane 6).

A greatly increased level of expression of μ was found in *E. Coli* B compared to HB101. Pulse chase analysis demonstrated that in *E. Coli* B, a similar level of μ protein was detected after a 60 minute chase (FIG. 7, lane 3) as was seen after the initial labelling period (FIG. 7, lane 1). In HB101, however, very little μ protein could be seen after a 10 minute chase (FIG. 7, lane 7), and none after 30 minutes (FIG. 7, lane 8), compared to the amount detected after the initial labelling period (FIG. 7, lane 5).

For pulse chase analysis, inductions were set up as described above, except that the medium used consisted of: proline (0.3 g/L), leucine (0.1 g/L), Difco methio-

nine assay medium (5 g/L), glucose (60 mg/L), thiamine (10 mg/L), $CaCl_2$ (22 mg/L), $MgSO_4$ (0.25 g/L)m and carbenicillin (0.1 g/L). During exponential growth cells were pulse labelled with 30 μCi/ml L-[$^{35}$S]methionine for 2 minutes, after which unlabelled methione (100 μg/ml) was added and the incubation continued for the times indicated.

Induced *E. Coli* B cells harbouring pNP14 when examined by phase contrast microscopy were found to contain inclusion bodies.

Expression of λ Light Chain in *E. Coli*

A fresh 1 ml overnight culture of *E. Coli* HB101 or RV308 containing the plasmid under study was grown in L Broth (Maniatis et al,, Molecular Cloning, Cold Spring Harbor Laboratory, 1982), supplemented with carbenicillin to 100 μg/ml.

A 1:100 dilution of this culture was made into M9 medium (Maniatis, 1982, op.cit.) supplemented with glucose, vitamin $B_1$, carbenicillin, leucine and proline and the cultures shaken at 37° for 5–6 hours. At this time $^{35}$S-methionine was added for 5–20 minutes. The cells were then harvested by centrifugation, lysed by boiling in 1% SDS for 2 minutes and diluted by addition of a buffer consisting of 2% Triton X-100, 50mM Tris pH 8, 0.15M NaCl and 0.1 mM EDTA. Immunoprecipitations were carried out by addition of antisera to aliquots of labelled *E. Coli* extracts and, after incubation at 4° overnight, immune complexes were isolated by binding to Staphylococcus aureus fixed cells. The complexes were dissociated by boiling in 60 mM Tris pH 6.8 buffer containing 10% glycerol, 3% SDS and 5% mercaptoethanol and the liberated proteins analysed on 10% or 12.5% acrylamide/SDS gels (Laemmli, UK. Nature, 227, 680–685, 1970). Gels were stained with Coomassie Brilliant blue to visualise the protein bands while labelled proteins were detected on Fuji-RX film by fluorography using 1M sodium salicylate.

HB101 cells containing pNP3 and other plasmids were grown under inducing conditions to an $OD_{600}$=0.6 and the proteins present examined by specific immunoprecipitation substantially as described above. The results obtained are given in FIG. 8, in which lanes 1 and 2 respectively were extracts from pCT54-19 and pNP3, immunoprecipitated with normal rabbit serum; lanes 3, 4 and 5 were extracts immunoprecipitated with rabbit anti-lambda serum and represent pNP4 (lane 3), pNP3 (lane 4) and pCT54-19 (lane 5). The position of unlabelled lambda protein from MOPC104E is indicated on the left hand side of FIG. 8. All of the plasmids produced a protein which reacted with rabbit anti-mouse λ light chain serum and comigrated with authentic $\lambda_1$ light chain from the mouse myeloma MOPC104E. pNP3 however produced the most of this protein (compare lane 4 with lanes 3 and 5 in FIG. 8). No such band was detected with control immunoprecipitations using normal rabbit serum (FIG. 8, lanes 1 and 2). Studies using brief pulses with $^{35}$S-methionine followed by chasing with excess cold methionine indicated that the recombinant λ light chain had a ½ life of about 20 minutes.

In vitro transcription/translation (Pratt et al, Nucleic Acids Research, 9, 4459–447, 1981) confirmed that pNP3 coded for a protein which comigrated with authentic λ light chain. This 25 Kd product was synthesized in vitro at a rate comparable to that of β-lactamase indicating that it is synthesised in vivo at a level of 0.5% of total *E. Coli* proteins. This figure is in good agreement with the percentage of recombinant λ product synthesised in vivo (0.4–2%) as determined from the following equation:

$$\% \text{ specific } CPM = \frac{100 \times (CPM \text{ with anti-}\lambda) - (CPM \text{ with normal serum})}{\text{total } CPM}$$

The procedure used to disrupt cells was as follows (Emtage J S et al, Proc. Natl. Acad. Sci., 80, 3671–3715, 1983). *E. Coli* HB101/pNP3 grown under inducing conditions were harvested and resuspended in 0.05M Tris pH 8, 0.233M NaCl, 5% glycerol containing 130 g/ml of lysozyme and incubated at 4° C. or room temperature for 20 minutes. Sodium deoxycholate was then added to a final concentration of 0.05% and 10 μg of DNAase 1 (from bovine pancreas) was added per g wet wt of *E. Coli.* The solution was incubated at 15° C. for 30 minutes by which time the viscosity of the solution had decreased markedly. The extract was centrifuged (at 10,000×g for 15 minutes for small volumes (1 ml) or 1 hour for larger volumes) to produce a soluble and an insoluble fraction.

For immunoprecipitations, the soluble fraction was diluted in the Triton-containing buffer described above and the insoluble fraction solubilised by boiling in 1% SDS followed by dilution in Triton-containing buffer. HB101 cells containing pNP3 or pNP4 were grown under inducing conditions, pulse labelled with [$^{35}$S]methionine, separated into soluble and insoluble fractions and analysed by sodium dodecyl sulfate polyacrylamide gel electrophoresis. The results obtained are shown in FIG. 9 in which lanes 1 and 3 correspond to the soluble fraction from HB101-pNP3 immunoprecipitated with normal rabbit serum and rabbit anti-lambda serum respectively; lanes 2 and 4 correspond to the insoluble fraction from HB101-pNP3 immunoprecipitated with normal rabbit serum and rabbit anti-lambda serum respectively, lanes 5 and 7 correspond to the soluble fraction from HB101-pNP4 immunoprecipitated with normal rabbit serum and rabbit anti-lambda serum respectively; lane 9 corresponds to the soluble fraction from HB101-pNP3, and lane 10 corresponds to the insoluble fraction from HB101-pNP3. The position of unlabelled lambda protein from MOPC104E is indicated on the left hand side of FIG. 9. When such a procedure was carried out using pNP3, the recombinant λ light chain protein was present in the insoluble fraction (FIG. 9, lane 4) rather than the soluble fraction (FIG. 9, lane 3). No 25 Kd band comigrating with authentic $\lambda_1$ light chain was present when either the soluble or insoluble fraction were immunoprecipitated using normal rabbit serum (FIG. 9, lanes 1 and 2). By inference it is likely that all Ig light chains will fractionate as in this specific example.

In the absence of specific immunoprecipitation a novel protein band was not visible from extracts of HB101 containing pNP3 nor was the λ protein found to accumulate. However, there was a dramatic difference when pNP3 was induced in the K12 strain E103s. In this strain λ protein was found to accumulate during induction until the cells reaches stationary phase (FIG. 10, lanes 3–5) to a level of about 150 times that found in HB101 as determined by an ELISA (enzyme linked immunosorbent assay). These cells were found to contain inclusion bodies which appeared refractile under light microscopy, a phenomenon characteristic of high

level expression of foreign proteins. An estimate of the pecentage of total *E. coli* protein represented by recombinant λ protein was obtained by separating the proteins by gel electrophoresis, staining them, with Coomassie blue and scanning the stained gel with a Joyce-Loebl chromoscan 3. This method showed that λ was the major protein present (FIG. 10, lane 5) and represented 13% or total *E. coli* protein. The λ protein had a half-life of 20 minute in HB101 but accumulated to very high levels in E103s, suggesting that lambda protein was much more stable in the latter strain. After cell lysis and centrifugation of HB101 or E103s containing pNP3, λ light chain was detected in the insoluble (FIG. 10, lanes 7 and 10) but not in the soluble fractions (FIG. 10, lanes 6), as determined by Coomassie blue staining. The identity of the major Coomassie blue stained band as λ protein was confirmed by Western blot analysis (FIG. 10, lanes 8–10). The presence of such immunoreactive bands was specific to pNP3 containing cells. When extracts from cells containing pCT70, a prochymosin expressing plasmid, were subjected to the same analysis no bands were detected. This more sensitive technique showed that a small amount of the λ protein was in the soluble fraction (FIG. 10, lane 9). The presence of a number of distinct immunoreactive proteins all smaller than full-length protein were also detected. These may result from proteolytic degradation of of λ protein, from premature termination of transcription or from internal initiation of translation.

Expression of μ and Lambda Polypeptides in the same Bacterial Cell

Each of the Ig μ and λ genes in expression plasmids were transformed into the same *E. Coli* cell to direct the synthesis of both Ig μ and λ polypeptides. In order to overcome plasmid incompatibility and provide a second antibiotic resistance marker, the trp promoter and λ sequences were excised from pNP3 on a Hind III-Bam HI fragment and inserted into the Hind III-Bam HI fragment of pACYC 184. The resultant plasmid pACYC λ caused the *E. coli* to grow very poorly. This weak growth was thought to result from read-through of RNA polymerase into the origin of replication. However, the inhibition of growth was virtually eliminated by the cloning in of the baceteriophage T7 transcriptional terminator at the Hind III site of plasmid pACYC λ.

This terminator functions in both orientations. The resultant plasmid pAC λ T7-1 has a chloroamphenicol resistance gene and an origin compatible with the pBR 322-derived origin on pNP14, the Ig μ expressing plasmid. Transformation of both plasmids in the same *E. Coli B* was achieved in two steps. Firstly pNP14 was introduced followed by pAC λ T7- I in two sequential transformations to give ampicillin and chloramphenicol resistant clones.

E. Coli B cells derived form this double-transformant clone showed the presence of inclusion bodies and two novel polypeptide bands on stained gels of the insoluble fraction after lysis. These two bands correspond both with immunological activity by Western blotting for Ig μ and Ig λ and in their expected molecular weights. It has thus been shown that the double-transformant clone expresses both the heterologous genes. This had not hitherto been shown.

The presence of λ light chain in the insoluble fraction was a useful purification step since it both concentrated the protein and separated if from the bulk of *E. Coli* soluble proteins.

For further purification of the λ light chain, the cell debris were dissolved in 10 mM Tris-HCl pH8.0, 25% formamide, 7M urea, 1 mM EDTA and 2 mM dithiothreitol. This material was loaded onto a DEAE Sephacel column (Pharmacia) (1×25 cm at a flow rate of 5 ml/hr) which had been equilibrated in 9M urea, 10 mM Tris-HCl pH 8.0, 1 mM EDTA and 2 mM DTT. The DEAE Sephacel column was developed using a 0–150 mM NaCl gradient in loading buffer. The eluted peak λ light chain immunoreactivity, corresponding to the major peak of protein, was diluted to a final concentration of 2.25M urea, 10 mM Tris-Hcl pH 8.0, 1 mM EDTA, 2 mM DTT and loaded onto an octylSepharose column (Pharmacia) (2.5×10 cm). Material was eluted by use of a urea gradient of 2.25–9M urea. The peak material was pooled, dialysed into ammonium bicarbonate and lyophilised. Following this step, only a single band of Coomassie blue stainable material corresponding to recombinant λ protein was visualised by SDS-PAGE.

The μ heavy chain was purified from 9M urea solubilised pellets by anion exchange chromatogrpahy and chromatofocussing (Pharmacia).

It was of great interest to determine whether the concomitant expression of μ and λ would lead to the formation of functional IgM. In order to determine this, extracts were made from *E. coli* containing both Ig μ and λ polypeptides and these tested for antigen binding. We used a two-site sandwich ELISA which detects μ chain binding to haptenalated bovine serum albumin (NIP-caproate-BSA).

In the NIP binding assay, bovine serum albumin (BSA) is reacted with an equimolar amount of NIP-Cap-N-hydroxy-succinamide at pH 7.5 in 10 mM phosphate buffer. The resulting NIP-Cap-BSA is separated from free NIP-Cap on a G-50 Sephadex column.

Microtitre plates (96 well Nunc Immuno Plate 1) are coated with 100 μl of a solution of 10 μg/ml NIP-BSA in sodium carbonate/sodium bicarbonate 0.1M, pH 9.6 buffer (coating buffer) overnight at 4° C.

The coated plates are then blocked for non-specific binding by addition of 100 μl of 0.5% casein in coating buffer (blocking buffer) and incubating at 37° C. for 1 hour.

The coated and blocked plates are then washed three times in 150 mM NaCl, 0.05% NP40, 20 mM Tris-HCl, pH 7.8 buffer (washing buffer).

The washed plates are shaken free of excess washing buffer and samples are added in their buffer or typically in 0.5% casein in washing buffer (sample buffer) to a 100 μl final volume.

In order to demonstrate the nature of the binding to NIP-BSA, samples for testing were supplemented with either NIP or NP is free solution at various concentrations (from 60 to 0.3 μM for NIP or from 600 to 3 μM for NP).

The plates with samples are then incubated at 37° C. for one hour and thereafter washed three times with washing buffer.

The washed plates are then innoculated with 100 μl of anti μ-peroxidase conjugate (1:1000 dilution; TAGO Inc) in sample buffer, and incubated for one hour at 37° C. The plates are then washed three times in washing buffer.

The washed plates are innoculated with 100 μl of 0.1M Na acetate-citrate, pH 6.0, 0.1 mg/ml tetramethyl-

benzidine, 13 mM $H_2O_2$ (peroxidase substrate) and incubated at room temperature for one hour. The reaction is terminated by the addition of 25 µl of 2.5M $H_2SO_4$.

The microtitre plates are then read in a plate reader (Dynatech) at 450 λm with a reference of 630 λm. The $A_{450}$ was related to the level of a standard protein, Bl-8 anti-NIP IgM.

This assay demonstrates sensitivity to 60 pg of Bl-8 IgM. The extracts were prepared as soluble and insoluble material. The insoluble material was solubilized in the same buffer used in lysis but containing 8M urea followed by its dilution for assay.

In order to obtain activity for the Ig µ and λ, extracts were made of the insoluble fraction and these dialysed into buffer conditions in which disulphide interchange will occur at a higher frequency.

Production of functional antibodies from *E. Coli* expressing both heavy and light chains was achieved by lysing the cells and clarifying the supernatant by centrifugation. The insoluble material was washed, followed by sonication (3 times for 3 minutes), and finally dissolved in 9M urea, 50 mM glycine-NaOH pH 10.8, 1 mM EDTA, and 20 mM 2-mercaptoethanol. This extract was dialysed for 40 hours against 3 changes of 20 vols. of 100 mM KCl, 50 mM glycine-NaOH pH 10.8, 5% glycerol, 0.05 mM EDTA, 0.5 mM reduced glutathione and 0.1 mM oxidised glutathione. The dialysate was cleared by centrifugation at 30,000 g for 15 minutes and loaded directly onto DEAE Sephacel, followed by development with a 0–0.5M KCl linear gradient in 10 mM Tris-HCl, 0.5 mM EDTA, pH 8.0.

The purified Ig µ and λ were treated as above, except that no anion exchange chromatography was carried out. The preparation was finally dialysed into phosphate buffered saline, 5% glycerol, 0.01% sodium azide and 0.5 mM EDTA pH 7.4.

The results from assays of material processed in this way indicated that some activity was obtained. The level of activity obtained in this way was too low to do any detailed studies on, so the resultant dialysate was purified by anion exchange chromatography (FIG. 11). This process resulted in the isolation of significant NIP-cap-BSA binding activity over that of background binding to BSA (FIG. 11). The assay of the fractions for the level of Ig µ, expressed as Bl-8 IgM equivalents demonstrated two peaks of activity. This was not found to correlate with full length Ig µ by Western blotting. The first peak observed may represent a fragment of Ig µ. The separation of NIP-CAP-BSA binding activity from the majority of full length Ig µ and protein indicates that the hapten binding activity is contained within a particular molecular species formed at low efficiency.

The processing of insoluble material obtained from Ig µ expression in *E. Coli* produced a similar IgM protein profile but without NIP-cap-BSA binding activity. This demonstrates that the activity recovered was a property of the combined immunoglobulin expression, not of some *E. Coli* factor, or of the Ig µ heavy chain alone.

Further studies of the characteristics of the hapten (NIP-cap-BSA) binding were carried out. As samples were diluted they showed less binding to hapten in a very similar way to the original antibody (FIG. 12). Free hapten was found to inhibit most of the binding activity in both indiluted and diluted samples. Using Bl-8 antibody as a standard for both IgM and hapten binding, the specific activity of the assembled antibody was calculated to be $1.4 \times 10^4$ gm/gm of IgM equivalents. This value demonstrates the inefficient recovery of activity, but possibly represents an underestimate of the specific activity due to an overestimate of full-length Ig µ in these fractions, as described above.

### Heteroclitic Nature of Recombined Antibody

Detailed specificity of binding to NIP-cap-BSA was investigated by comparing the assembled antibodies with Bl-8 IgM in the presence of free NIP-cap and NP-cap (FIG. 13). Both Bl-8 IgM and the assembled antibodies showed that higher NP-cap than NIP-cap concentrations were required to inhibit NIP-cap-BSA binding.

The heteroclitic nature is demonstrated by the molar ratio of NIP to NP at 50% inhibition. The concentrations of NIP and NP at 50% inhibition (I50) were found to be similar for both Bl-8 and the assembled antibodies as shown in Table 2. Also the NP I50/NIP I50 ratios were similar (Table 2).

TABLE 2

Hapten concentration at 50% inhibition (I50) of binding of antibodies to NIP-cap-BSA solid phase. SD = Deviation.

| | NIP I50 uM | NP I50 uM | NP I50/ NIP I50 |
|---|---|---|---|
| Bl-8 IgM | 0.13 (SD, 0.05) | 3.7 (SD, 2.9) | 29 |
| Fraction 26 | 0.24 (SD, 0.09) | 1.9 (SD, 0.4) | 6 |
| Fraction 27 and 28 | 0.11 (SD, 0.02) | 1.1 (SD, 0.3) | 10 |
| Purified µ and λ | 0.4 | 0.84 | 22 |

It has thus been shown that not only is it possible to express µ and λ proteins having intact variable domains, but also that it is possible to express both µ and λ proteins on compatible plasmids in the same cell. This latter has not hitherto been disclosed or even suggested. Moreover, it proved possible to derive functional Ig molecules from *E. Coli* cells which expressed both µ and λ proteins.

It has thus been shown that the process of the present invention produces a functional Ig molecule by recombinant DNA techniques.

### Construction of Expression Plasmids for Yeast

The plasmids used for expression in yeast (*Saccharomyces cerevisiae*) are based on pBR322 and the yeast 2 micron plasmid. These plasmids are the subject of copending European Patent Application EP 0 073 635, the disclosure of which is incorporated hereby reference. The yeast phosphoglycerate kinase gene (PGK) provides the 5' sequence necessary for initiation of transcription and insertion of genes can be made at the unique BgIII site in the plasmid pMA 3013 described in the above mentioned European patent application. This plasmid has now been renamed pMA91 as is so referred to hereinafter.

(a) met-mu (µ)

BglII and BclI produce compatible 5'-GATC ends. The met-µ gene from pNP2 was excised on a partial BclI fragment and ligated into the unique BglII site of pMA91.

(b) Pre-mu (µ)

The plasmid pCT54 u containing the full lengths pre-µ cDNA was digested with Hind III. This cuts at the 3' side of the µ cDNA. This Hind III site was changed to a BclI site by incubation with $T_4$ DNA polymerase in the presence of all 4 nucleotides. The linker R107 of sequence TTTTGATCAAAA, which contains an internal BclI was ligated to the DNA obtained above. After ligation one aliquot of the resultant

DFNA was digested with BcII and AccI and the μ AccI-BcII fragment was isolated from the resultant mixture by gel electrophoresis. A separate aliquot of the resultant DNA was digested with MboII and ligated with chemically synthesised oligonucleotide linkers R121 and R112 which have cohesive BcII and MboII ends.

R121 5' GATCAATGGGATGGAGCTGT 3'

R112 5' TTACCCTACCTCGAC 3'

The ligation reaction was terminated and the resultant DNA digested with AccI to give a μ MboII-AccI fragment which was isolated from the resultant mixture by gel electrophoresis on a 5% polyacrylamide gel.

The two μ fragments obtained above were ligated together and then digested with BcII to eliminate unwanted ligation products after which the resultant pre-μ DNA was ligated to BgIII cut plasmid pMA91.

The resultant ligation mix was used to transform *E. Coli* strain HB101 to ampicillin resistance. A colony of the transformed bacteria was isolated and was found to contain a plasmid exhibiting the predicted enzyme digestion pattern. The 5' end of the inserted DNA from this plasmid was sequenced and shown to have the anticipated sequence for a pre-μ cDNA.

(c) met-lambda (λ)

The met-λ DNA was cloned into the BgIII site of plasmid pMA91. Plasmid pCT54 Clone 1 was cut with Hind III to the 3' side of the met-λ cDNA and this cleavage site was altered to a BclI site in a similar manner as previously described for pNP2. Following this the plasmid DNA was cut 5' of the λ gene at the BclI site and the resultant λ DNA was cloned into the BglII site of pMA91.

(d) Pre-lambda (λ)

Pre-λ cDNA was reconstructed into pMA 91 as follows. The plasmid pCT54 was digested with BclI and Hind III and the resultant vector DNA was isolated by gel electrophoresis and ligated together with two synthetic oligonucleotides, R162 and R163, and the two fragments from plasmid pAT λ 1-15.

R162 5' GATCAATGGCCTGGATT 3'

R163 5' GTGAAATCCAGGCCATT 3'

These fragments were produced by digesting pAT λ 1-15 with FokI and Hind III and isolating the 5'300 base pair FokI fragment and the 3' 600 base pair FokI-Hind III fragment by gel electrophoresis. The resultant ligation mixture was used to transform *E. Coli* strain HB101 to ampicillin resistance and a colony of bacteria containing a plasmid having the predicted correct restriction enzyme digestion pattern was isolated. The 5' end of the inserted DNA was sequenced and found to have the anticipated sequence of a pre-λ cDNA. This plasmid was digested with Hind III and the resultant Hind III cleaved ends converted to a BclI site by blunting with $T_4$ polymerase and ligating with the linker R107. The resultant plasmid was then digested with BclI and the pre-λ cDNA isolated on a BclI fragment by gel electrophoresis. This BclI fragment was then ligated to BglI cut pMA91 to give a pMA 91 plasmid containing the full length pre-λ cDNA.

Expression of Immunoglobulin Genes in Yeast

The pMA91 derivative plasmids containing the pre-λ and pre-μ genes as prepared above were used to transform *Saccharomyces cerevisiae* yeast host organisms and the pre-λ and pre-μ genes were expressed by the transformed cells.

*Saccharomyces cerevisiae* strain MD46 when transformed with pMA91 pre-λ or pMA91 pre-μ gave rise to colonies which expressed immunoreactive proteins as revealed on Western blots. Yeast cells containing plasmid pMA91 pre-λ produced a protein which reacted with anti-λ antiserum and co-migrated on polyacrylamide gels with bacterially synthesised mature λ. Similarly yeast cells containing pMA 91 pre-μ produced a protein which reacted with anti-μ antiserum and co-migrated on polyacrylamide gels with bacterially synthesised mature λ protein. These observations indicate that both pre-μ and pre-μ are being processed to the corresponding mature proteins within the yeast host cell environment.

Additionally the λ protein product (but not the λ protein) was shown to be glycosylated. Cells were incubated in the presence or absence of tunicamycin at a concentration of 15 μg/ml. This compound specifically arrests the N-linked glycosylation of proteins. Cell extracts derived from cells incubated in the absence of tunicamycin showed higher molecular weight bands (as revealed by Western blotting) whilst extracts from cells incubated in the presence of tunicamycin showed no such higher molecular weight bands.

When cells were lysed with glass beads and the soluble and insoluble fractions examined it was found that the μ and λ proteins were exclusively in the insoluble fractions, as determined by Western blotting.

Secretion

After incubation transformed yeast cells were spun down and 1 ml volumes of supernatant were removed and passed through BSA-coated 0.2 μM Millipore filters to remove any remaining cellular material. ELISA assays for μ and λ protein were then carried out on the filtered supernatants. Only supernatants from pMA91 pre-λ harbouring cells showed detectable levels of immunoglobulin protein. Increased amounts of λ protein was detected in the supernatant when cells were grown in minimal medium to $OD_{660}$=0.2 and then spun down and resuspended in YPAB and harvested at $OD_{660}$=1-.0-1.5. Thus the λ protein but not the μ protein is secreted from yeast cells.

Intracellular Location

After incubation cells containing pMA91 pre-μ were converted to spheroplasts and fixed in 5% acetic acid/95% ethanol (v/v) and incubated with fluorescein conjugated goat anti-mouse μ. The fixed cells were examined by fluorescent microscopy and the μ protein was found to be localised in the periphery of the spheroplasts and especially in vacuoles.

Expression of both μ and λ Proteins in the Same Cells

In order to express both genes in the same host cells it was necessary to provide compatible plasmids for use in transformation. The pre-λ gene was excised from pMA91 pre-λ on a Hind III fragment and inserted into the Hind III site of plasmid pLG89 (Griti L, and Davies J, Gene, 25 179-188, 1983). This plasmid contains a ura3 marker which can be used as a positive selection for

transformed host cells. A convenient ura3 host organism is *S. cerevisiae* strain X4003-5B. Both plasmids, pMA91 pre-μ and pLG89 pre-λ, were transformed into this strain, and colonies were grown which contained together both the ura3 and leu2 markers. After incubation of the transformed cells both λ and μ proteins together were detected in the same cultures of X4003-5B using ELISA techniques. Levels of expression were comparable to those obtained for the individual genes in MD46 cells and for the λ gene alone in X4000-5B.

In addition, to check for assembly of the λ and μ proteins in vivo the following procedure was followd.

After the growth to an $OD_{660}$≃1, the transformed X4003-5B cell were spun down and resuspended in buffer, either 5 mM borate buffer at pH 8.0 or phosphate buffer at pH 5.8 either with or without detergent (e.g. 0.5% Triton X). The suspended cells were then lysed by vortexing with glass heads in buffer as above and the insoluble material was spun down. After centrifugation aliquots of the supernatant were assayed in a NIP binding assay (as described previously for assembled *E. Coli* μ and λ proteins). Specific antigen binding activity was detected in the supernatant and this activity was shown to be specifically competed out by free NIP (the specific antigen). These results indicated that μ and λ protein were expressed within the X4003-5 B cells and assembled into functional immunoglobulin molecules in vivo.

In the above experiments the culture medium used for incubating the transformed cells was yeast minimal medium (containing, per liter, 6.7 g DIFCO yeast nitrogen base without amino acids, 10 g glucose, and 200 mg each of histidine, tryptophan, methionine and adenine). When the λ protein alone was being expressed the medium contained in addition 200 mg/l of leucine, and when the μ protein alone was being expressed the medium contained in addition 200 mg/l of uracil.

We claim:

1. A process for producing an Ig molecule or an immunologially functional Ig fragment comprising at least the variable domains of the Ig heavy and light chains, in a single host cell, comprising the steps of:

(i) transforming said single host cell with a first DNA sequence encoding at least the variable domain of the Ig heavy chain and a second DNA sequence encoding at least the variable domain of the Ig light chain, and

(ii) independently expessing said first DNA sequence and said second DNA sequence so that said Ig heavy and light chains are produced as separate molecules in said transformed single host cell.

2. The process according to claim 1 wherein said first and second DNA sequences are present in different vectors.

3. The process according to claim 1 wherein said first and second DNA sequences are present in a single vector.

4. A process according to claim 2 wherein the or each vector is a plasmid.

5. A process according to claim 4, wherein the plasmid is col E1, pcR1, pBR322, RP4 or phage DNA.

6. A process according to claim 1 wherein the host cell is a baceterium or a yeast.

7. A process according to claim 6, wherein the host cell is *E. Coli, B. subtilis* or *S. cerevisiae.*

8. A process according to claim 7, wherein the host cell is *E. Coli* strain HB101, X1776, X2887, PS410, MRC 1 RV308, B or E1035.

9. A process according to claim 1 wherein the Ig heavy and light chains are expressed in the host cell and secreted therefrom as an immunologically functional Ig molecule or Ig fragment.

10. A process according to claim 1 wherein the Ig heavy and light chains are produced in insoluble or membrane bound form and are solubilised and allowed to refold in solution to form an immunologically functional Ig molecule or Ig fragment.

11. A process according to claim 1, wherein the DNA sequences code for the complete Ig heavy and light chains.

12. A process according to claim 1, wherein said first or said second DNA sequence further encodes at least one constant domain, wherein the constant domain is derived from the same source as the variable domain to which it is attached.

13. A process according to claim 1, wherein said first or said second DNA sequence further encodes at least one constant domain, wherein the constant domain is derived from a source different from that from which the variable domain to which it is attached is derived.

14. A process according to claim 1, wherein said first and second DNA sequences are derived from one or more monoclonal antibody producing hybridomas.

15. A vector comprising a first DNA sequence encoding at last a variable domain of an Ig heavy chain and a second DNA sequence encoding at least a variable domain of an Ig light chain wherein said first DNA sequence and said second DNA sequence are located in said vector at different insertion sites.

16. A vector according to claim 15, which is a plasmid.

17. A host cell transformed with a vector according to claims 15.

18. A transformed host cell comprising at least two vectors, at least one of said vectors comprising a DNA sequence encoding at least a variable domain of an Ig heavy chain and at least another one of said vectors comprising a DNA sequence encoding at least the variable domain of an Ig light chain.

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# United States Patent [19]

**Cabilly et al.**

[11] **Patent Number: 4,816,567**

[45] **Date of Patent: Mar. 28, 1989**


[54] **RECOMBINANT IMMUNOGLOBIN PREPARATIONS**


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[21] Appl. No.: **483,457**

[22] Filed: **Apr. 8, 1983**

[51] **Int. Cl.**[4] ..... **C07K 15/14**; C07K 15/06; C12P 21/00; C12N 15/00; C12N 1/20

[52] **U.S. Cl.** ..... **530/387**; 435/68; 435/172.3; 435/320; 435/252.3; 435/252.31; 435/252.33; 435/252.34; 935/10; 935/15; 935/29; 935/73; 530/388

[58] **Field of Search** ..... 435/68, 172.3, 240, 435/253, 172.2, 317, 320; 260/112 B; 536/27; 935/11, 15, 27, 29, 73; 530/387, 388



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*Primary Examiner*—Jayme Huleatt

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[57] **ABSTRACT**

Altered and native immunoglobulins, including constant-variable region chimeras, are prepared in recombinant cell culture. The immunoglobulins contain variable regions which are immunologically capable of binding predetermined antigens. Methods are provided for refolding directly expressed immunoglobulins into immunologically active form.


**7 Claims, 15 Drawing Sheets**

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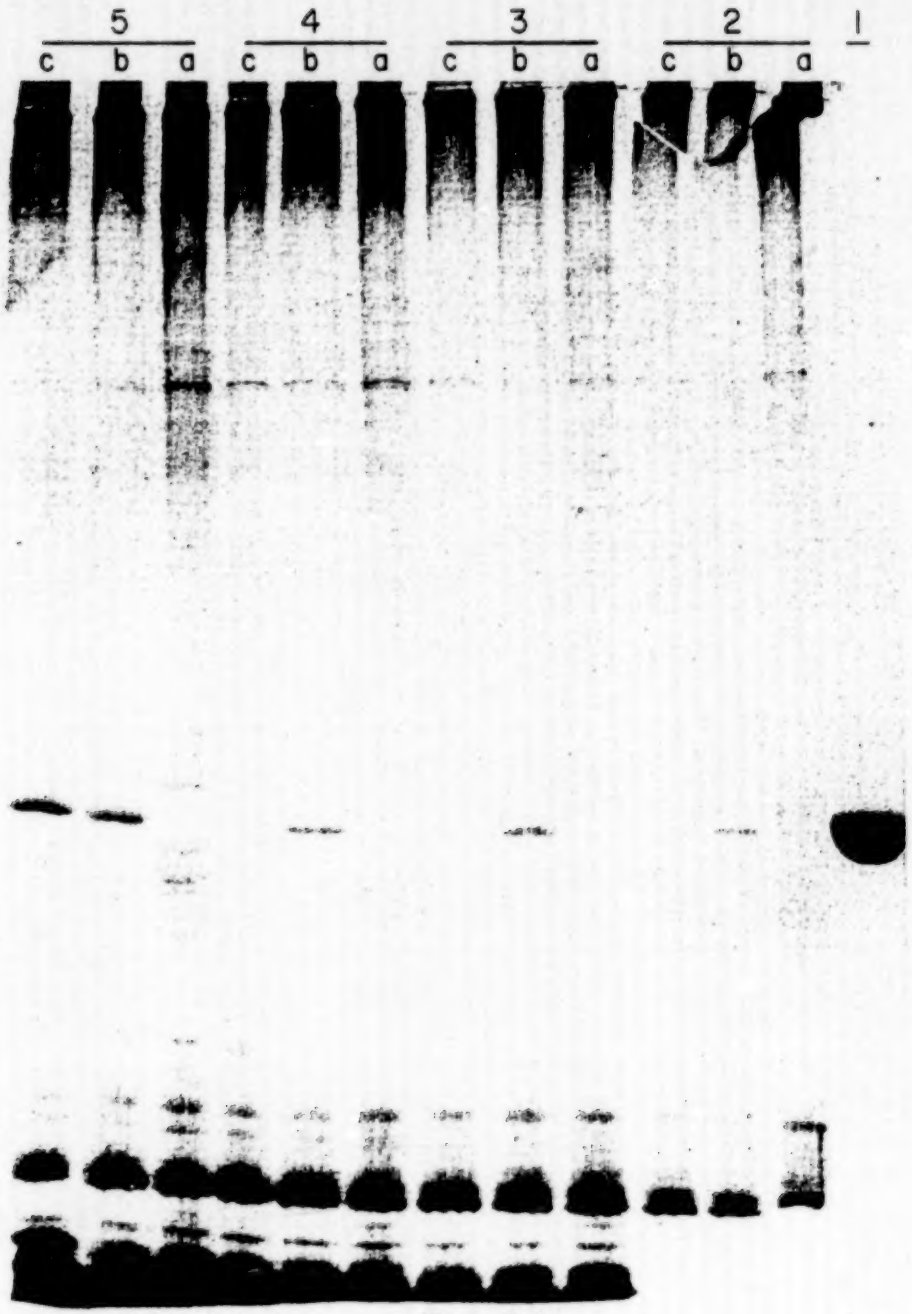


Fig. 8A.

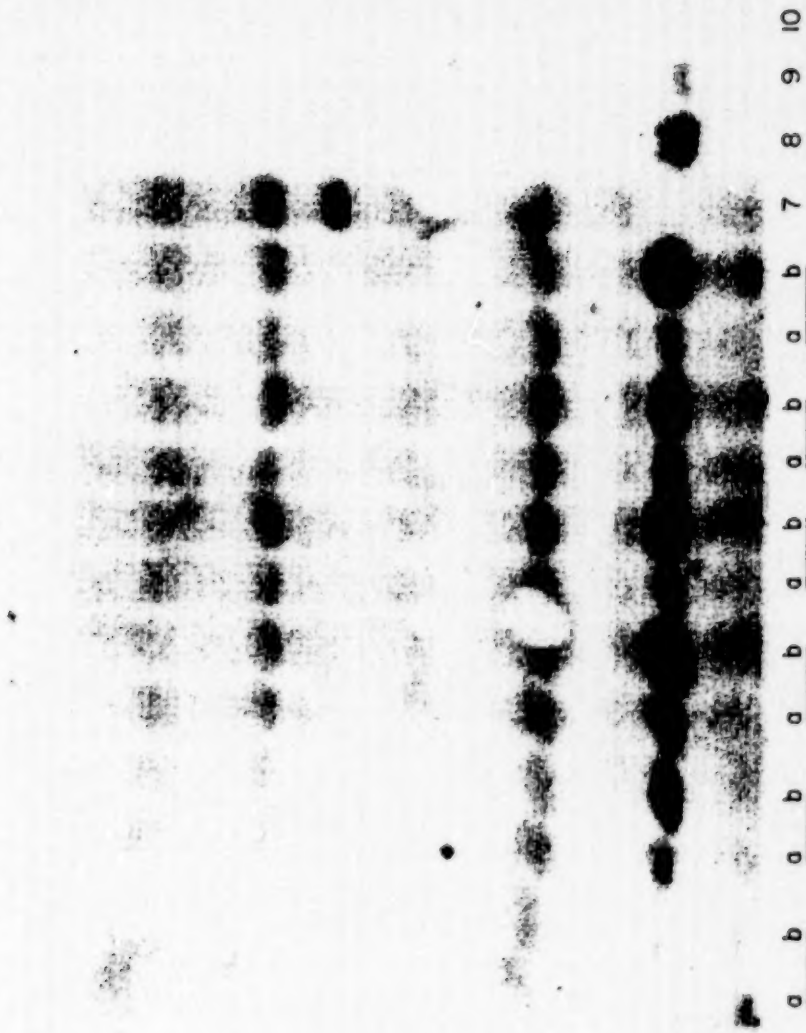


Fig. 8B.

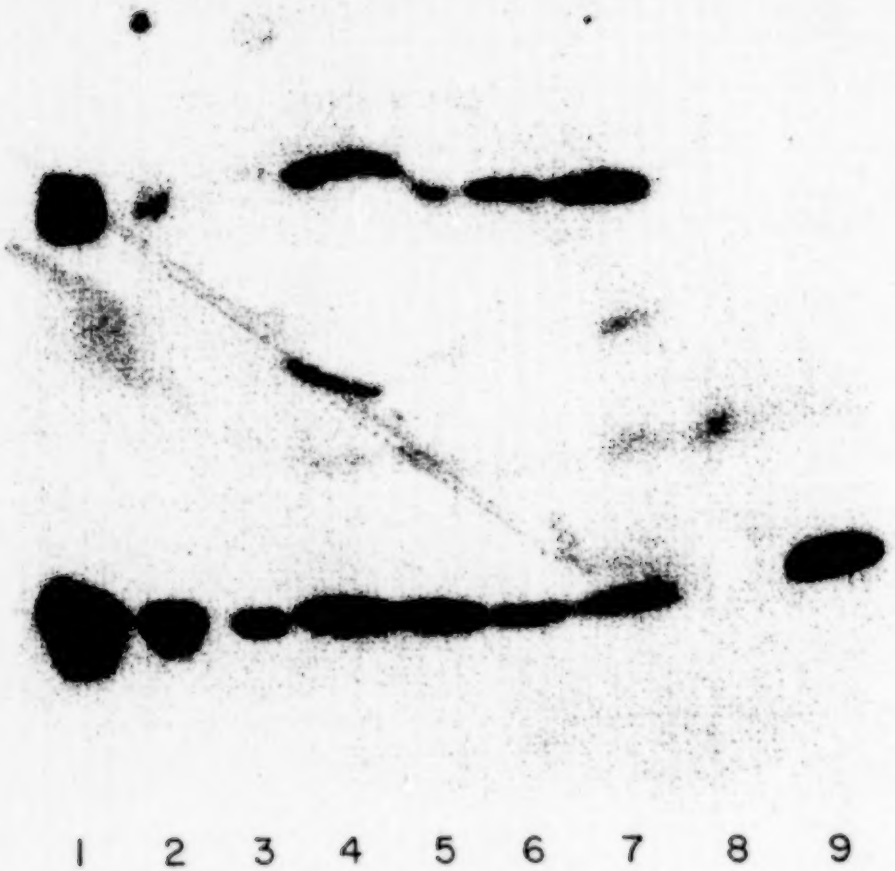


Fig. 8C.

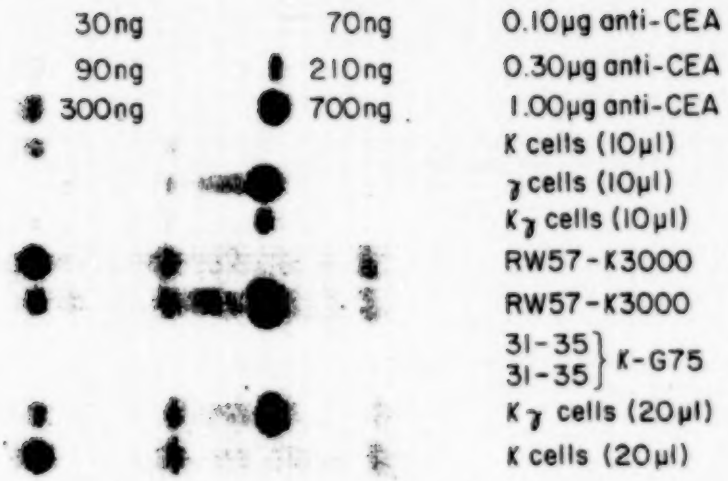
30ng
70ng
0.10μg anti-CEA
90ng
210ng
0.30μg anti-CEA
300ng
700ng
1.00μg anti-CEA
K cells (10μl)
γ cells (10μl)
Kγ cells (10μl)
RW57-K3000
RW57-K3000
31-35
31-35
K-G75
Kγ cells (20μl)
K cells (20μl)

Fig. 9.

# RECOMBINANT IMMUNOGLOBIN PREPARATIONS

## BACKGROUND OF THE INVENTION

This invention relates to the field of immunoglobulin production and to modification of naturally occuring immunoglobulin amino acid sequences. Specifically, the invention relates to using recombinant techniques to produce both immunoglobulins which are analogous to those normally found in vertebrate systems and to take advantage of these gene modification techniques to construct chimeric or other modified forms.

A. Immunoglobulins and Antibodies

Antibodies are specific immunoglobulin polypeptides produced by the vertebrate immune system in response to challenge by foreign proteins glycoproteins, cells, or other antigenic foreign substances. The sequence of events which permits the organism to overcome invasion by foreign cells or to rid the system of foreign substances is at least partially understood. An important part of this process is the manufacture of antibodies which bind specifically to a particular foreign substance. The binding specificity of such polypeptides to a particular antigen is highly refined, and the multitude of specificities capable of being generated by the individual vertebrate is remarkable in its complexity and variability. Thousands of antigens are capable of eliciting responses, each almost exclusively directed to the particular antigen which elicted it.

Immunoglobulins include both antibodies, as above described, and analogous protein substances which lack antigen specificity. The latter are produced at low levels by the lymph system and in increased levels by myelomas.

A.1 Source and Utility

Two major sources of vertebrate antibodies are presently utilized—generation in situ by the mammalian B lymphocytes and in cell culture by B-cell hybrids. Antibodies are made in situ as a result of the differentiation of immature B lymphocytes into plasma cells, which occurs in response to stimulation by specific antigens. In the undifferentiated B cell, the portions of DNA coding for the various regions on the immunoglobulin chains are separated in the genomic DNA. The sequences are reassembled sequentially prior to transcription. A review of this process has been given by Gough, *Trends in Biochem Sci.* 6: 203 (1981). The resulting rearranged genome is capable of expression in the mature B lymphocyte to produce the desired antibody. Even when only a single antigen is introduced into the sphere of the immune system for a particular mammal, however, a uniform population of antibodies does not result. The in situ immune response to any particular antigen is defined by the mosaic of responses to the various determinants which are present on the antigen. Each subset of homologous antibody is contributed by a single population of B cells—hence in situ generation of antibodies is "polyclonal".

This limited but inherent heterogeneity has been overcome in numerous particular cases by use of hybridoma technology to create "monoclonal" antibodies (Kohler, et al., *Eur. J. Immunol.*, 6: 511 (1976)). In this process, splenocytes or lymphocytes from a mammal which has been injected with antigen are fused with a tumor cell line, thus producing hybrid cells or "hybridomas" which are both immortal and capable of producing the genetically coded antibody of the B cell. The hybrids thus formed are segregated into single genetic strains by selection, dilution, and regrowth, and each strain thus represents a single genetic line. They therefore produce immunoreactive antibodies against a desired antigen which are assured to be homogenous, and which antibodies, referencing their pure genetic parentage, are called "monoclonal". Hybridoma technology has to this time been focused largely on the fusion of murine lines, but human-human hybridomas (Olsson, L. et al., *Proc. Natl. Acad. Sci. (USA)*, 77: 5429 (1980)); human-murine hybridomas (Schlom, J., et al. (ibid) 77: 6841 (1980)) and several other xenogenic hybrid combinations have been prepared as well. Alternatively, primary, antibody producing, B cells have been immortalized in vitro by transformation with viral DNA.

Polyclonal, or, much more preferably, monoclonal, antibodies have a variety of useful properties similar to those of the present invention. For example, they can be used as specific immunoprecipitating reagents to detect the presence of the antigen which elicited the initial processing of the B cell genome by coupling this antigen-antibody reaction with suitable detection techniques such as labeling with radioisotopes or with enzymes capable of assay (RIA, EMIT, and ELISA). Antibodies are thus the foundation of immuno diagnostic tests for many antigenic substances. In another important use, antibodies can be directly injected into subjects suffering from an attack by a substance or organism containing the antigen in question to combat this attack. This process is currently in its experimental stages, but its potential is clearly seen. Third, whole body diagnosis and treatment is made possible because injected antibodies are directed to specific target disease tissues, and thus can be used either to determine the presence of the disease by carrying with them a suitable label, or to attack the diseased tissue by carrying a suitable drug.

Monoclonal antibodies produced by hybridomas, while theoretically effective as suggested above and clearly preferable to polyclonal antibodies because of their specificity, suffer from certain disadvantages. First, they tend to be contaminated with other proteins and cellular materials of hybridoma, (and, therefore, mammalian) origin. Second, hybridoma lines producing monoclonal antibodies tend to be unstable and may alter the structure of antibody produced or stop producing antibody altogether (Kohler, G., et al., *Proc. Antl. Acad. Sci (USA)* 77: 2197 (1980); Morrison, S. L., *J. Immunol.* 123: 793 (1979)). The cell line genome appears to alter itself in response to stimuli whose nature is not currently known, and this alteration may result in production of incorrect sequences. Third, both hybridoma and B cells inevitably produce certain antibodies in glycosylated form (Melchers, F., *Biochemistry*, 10: 653 (1971)) which, under some circumstances, may be undesirable. Fourth, production of both monoclonal and polyclonal antibodies is relatively expensive. Fifth, and perhaps most important, production by current techniques (either by hybridoma or by B cell response) does not permit manipulation of the genome so as to produce antibodies with more effective design components than those normally elicited in response to antigens from the mature B cell in situ. The antibodies of the present invention do not suffer from the foregoing drawbacks, and, furthermore, offer the opportunity to provide molecules of superior design.

Even those immunoglobulins which lack the specificity of atibodies are useful, although over a smaller spectrum of potential uses than the antibodies themselves. In presently understood applications, such immunoglobulins are helpful in protein replacement therapy for globulin related anemia. In this context, an inability to bind to antigen is in fact helpful, as the therapeutic value of these proteins would be impaired by such functionality. At present, such non-specific antibodies are derivable in quantity only from myeloma cell cultures suitably induced. The present invention offers an alternative, more economical source. It also offers the opportunity of cancelling out specificity by manipulating the four chains of the tetramer separately.

A.2 General Structure Characteristics

The basic immunoglobin structural unit in vertebrate systems is now well understood (Edelman, G. M., *Ann. N.Y. Acad. Sci.*, 190: 5 (1971)). The units are composed to two identical light polypeptide chains of molecular weight approximately 23,000 daltons, and two identical heavy chains of molecular weight 53,000-70,000. The four chains are joined by disulfide bonds in a "Y" configuration wherein the light chains bracket the heavy chains starting at the mouth of the Y and continuing through the divergent region as shown in FIG. 1. The "branch" portion, as there indicated, is designated the Fab region. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, with some subclasses among them, and the nature of this chain, as it has a long constant region, determines the "class" of the antibody as IgG, IgM, IgA, IgD, or IgE. Light chains are classified as either kappa or lambda. Each heavy chain class can be prepared with either kappa or lambda light chain. The light and heavy chains are covalently bonded to each other, and the "tail" portions of the two heavy chains are bonded to each other by covalent disulfide linkages when the immunoglobulins are generated either by hybridomas or by B cells. However, if non-covalent association of the chains can be effected in the correct geometry, the aggregate will still be capable of reaction with antigen, or of utility as a protein supplement as a non-specific immunoglobulin.

The amino acid sequence runs from the N-terminal end at the top of the Y to the C-terminal end at the bottom of each chain. At the N-terminal end is a variable region which is specific for the antigen which elicited it, and is approximately 100 amino acids in length, there being slight variations between light and heavy chain and from antibody to antibody. The variable region is linked in each chain to a constant region which extends the remaining length of the chain. Linkage is seen, at the genomic level, as occuring through a linking sequence known currently as the "J" region in the light chain gene, which encodes about 12 amino acids, and as a combination of "D" region and "J" region in the heavy chain gene, which together encode approximately 25 amino acids.

The remaining portions of the chain are referred to as constant regions and within a particular class do not to vary with the specificity of the antibody (i.e., the antigen eliciting it).

As stated above, there are five known major classes of constant regions which determine the class of the immunoglobulin molecule (IgG, IgM, IgA, IgD, and IgE corresponding to $\gamma$, $\mu$, $\alpha$, $\delta$, and $\epsilon$ heavy chain constant regions). The constant region or class determines subsequent effector function of the antibody, including activation of complement (Kabat, E. A., *Structural Concepts in Immunology and Immunochemistry*, 2nd Ed., p. 413-436, Holt, Rinehart, Winston (1976)), and other cellular responses (Andrews, D. W., et al., *Clinical Immunobiology*, pp 1-18, W. B. Sanders (1980); Kohl, S., et al., *Immunology*, 48: 187 (1983)); while the variable region determines the antigen with which it will react.

B. Recombinant DNA Technology

Recombinant DNA technology has reach sufficient sophistication that it includes a repertoire of techniques for cloning and expression of gene sequences. Various DNA sequences can be recombined with some facility, creating new DNA entities capable of producing heterologous protein product in transformed microbes and cell cultures. The general means and methods for the in vitro ligation of various blunt ended or "sticky" ended fragments of DNA, for producing expression vectors, and for transforming organisms are now in hand.

DNA recombination of the essential elements (i.e., an origin of replication, one or more phenotypic selection characteristics, expression control sequence, heterologous gene insert and remainder vector) generally is performed outside the host cell. The resulting recombinant replicable expression vector, or plasmid, is introduced into cells by transformation and large quantities of the recombinant vehicle is obtained by growing the transformant. Where the gene is properly inserted with reference to portions which govern the transcription and translation of the encoded DNA message, the resulting expression vector is useful to produce the polypeptide sequence for which the inserted gene codes, a process referred to as "expression." The resulting product may be obtained by lysis, if necessary, of the host cell and recovery of the product by appropriate purifications from other proteins.

In practice, the use of recombinant DNA technology can express entirely heterologous polypeptides—so-called direct expression—or alternatively may express a heterologous polypeptide fused to a portion of the amino acid sequence of a homologous polypeptide. In the latter cases, the intended bioactive product is sometimes rendered bioinactive within the fused, homologous/heterologous polypeptide until it is cleaved in an extracellular environment.

The art of maintaining cell or tissue cultures as well as microbial systems for studying genetics and cell physiology is well established. Means and methods are available for maintaining permanent cell lines, prepared by successive serial transfers from isolated cells. For use in research, such cell lines are maintained on a solid support in liquid medium, or by growth in suspension containing support nutriments. Scale-up for large preparations seems to pose only mechanical problems.

## SUMMARY OF THE INVENTION

The invention relates to antibodies and to non-specific immunoglobulins (NSIs) formed by recombinant techniques using suitable host cell cultures. These antibodies and NSIs can be readily prepared in pure "monoclonal" form. They can be manipulated at the genomic level to produce chimeras of variants which draw their homology from species which differ from each other. They can also be manipulated at the protein level, since all four chains do not need to be produced by the same cell. Thus, there are a number of "types" of immunoglobulins encompassed by the invention.

First, immunoglobulins, particularly antibodies, are produced using recombinant techniques which mimic

the amino acid sequence of naturally occuring antibodies produced by either mammalian B cells in situ, or by B cells fused with suitable immortalizing tumor lines, i.e., hybridomas. Second, the methods of this invention produced, and the invention is directed to, immunoglobulins which comprise polypeptides not hitherto found associated with each other in nature. Such reassembly is particularly useful in producing "hybrid" antibodies capable of binding more than one antigen; and in producing "composite" immunoglobuins wherein heavy and light chains of different origins essentially damp out specificity. Third, by genetic manipulation, "chimeric" antibodies can be formed wherein, for example, the variable regions, correspond to the amino acid sequence from one mammalian model system, whereas the constant region mimics the amino acid sequence of another. Again, the derivation of these two mimicked sequences may be from different species. Fourth, also by genetic manipulation, "altered" antibodies with improved specificity and other characteristics can be formed.

Two other types of immunoglobulin-like moieties may be produced: "univalent" antibodies, which are useful as homing carriers to target tissues, and "Fab proteins" which include only the "Fab" region of an immunoglobulin molecule i.e, the branches of the "Y". These univalent antibodies and Fab fragments may also be "mammalian" i.e., mimic mammalian amino acid sequences; novel assemblies of mammalian chains, or chimeric, where for example, the constant and variable sequence patterns may be of different origin. Finally, either the light chain or heavy chain alone, or portions thereof, produced by recombinant techniques are included in the invention and may be mammalian or chimeric.

In other aspects, the invention is directed to DNA which encodes the aforementioned NSIs, antibodies, and portions thereof, as well as expression vectors or plasmids capable of effecting the production of such immunoglobulins in suitable host cells. It includes the host cells and cell cultures which result from transformation with these vectors. Finally, the invention is directed to methods of producing these NSIs and antibodies, and the DNA sequences, plasmids, and transformed cells intermediate to them.

## BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a representation of the general structure of immunoglobulins.

FIG. **2A** and **2B** show the detailed sequence of the cDNA insert of pK17G4 which encodes kappa anti CEA chain.

FIG. **3** shows the coding sequence of the fragment shown in FIG. **2**, along with the corresponding amino acid sequence.

FIGS. **4A**, **4B** and **4C** show the combined detailed sequence of the cDNA inserts of pγ298 and pγ11 which encode gamma anti CEA chain.

FIGS. **5A** and **5B** show the corresponding amino acid sequence encoded by the fragment in FIG. **4**.

FIGS. **6** and **7** outline the construction of expression vectors for kappa and gamma anti-CEA chains respectively.

FIGS. **8A**, **8B**, and **8C** show the results of sizing gels run on extracts of *E. coli* expressing the genes for gamma chain, kappa chain, and both kappa and gamma chains respectively.

FIG. **9** shows the results of western blots of extracts of cells transformed as those in FIGS. **8**.

FIG. **10** shows a standard curve for ELISA assay of anti CEA activity.

FIGS. **11** and **12** show the construction of a plasmid for expression of the gene encoding a chimeric heavy chain.

FIG. **13** shows the construction of a plasmid for expression of the gene encoding the Fab region of heavy chain.

## DETAILED DESCRIPTION

A. Definitions

As used herein, "antibodies" refers to tetramers or aggregates thereof which have specific immunoreactive activity, comprising light and heavy chains usually aggregated in the "Y" configuration of FIG. **1**, with or without covalent linkage between them; "immunoglobulins" refers to such assemblies whether or not specific immunoreactive activity is a property. "Non-specific immunoglobulin" ("NSI") means those immunoglobulins which do not possess specificity—i.e., those which are not antibodies.

"Mammalian antibodies" refers to antibodies wherein the amino acid sequences of the chains are homologous with those sequences found in antibodies produced by mammalian systems, either in situ, or in hybridomas. These antibodies antibodies mimic antibodies which are otherwise capable of being generated, although in impure form, in these traditional systems.

"Hybrid antibodies" refers to antibodies wherein chains are separately homologous with reference mammalian antibody chains and represent novel assemblies of them, so that two different antigens are precipitable by the tetramer. In hybrid antibodies, one pair of heavy and light chain is homologous to antibodies raised against one antigen, while the other pair of heavy and light chain is homologous to those raised against another antigen. This results in the property of "divalence" i.e., ability to bind two antigens simultaneously. Such hybrids may, of course, also be formed using chimeric chains, as set forth below.

"Composite" immunoglobulins means those wherein the heavy and light chains mimic those of different species origins or specificities, and the resultant is thus likely to be a non-specific immunoglobulin (NSI), i.e.—lacking in antibody character.

"Chimeric antibodies" refers to those antibodies wherein one portion of each of the amino acid sequences of heavy and light chains is homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular class, while the remaining segment of the chains is homologous to corresponding sequences in another. Typically, in these chimeric antibodies, the variable region of both light and heavy chains mimics the variable regions of antibodies derived from one species of mammals, while the constant portions are homologous to the sequences in antibodies derived from another. One clear advantage to such chimeric forms is that, for example, the variable regions can conveniently be derived from presently known sources using readily available hybridomas or B cells from non human host organisms in combination with constant regions derived from, for example, human cell preparations. While the variable region has the advantage of ease of preparation, and the specificity is not affected by its source, the constant region being human, is less likely to elicit an immune response from

a human subject when the antibodies are injected than would the constant region from a non-human source.

However, the definition is not limited to this particular example. It includes any antibody in which either or both of the heavy or light chains are composed of combinations of sequences mimicking the sequences in antibodies of different sources, whether these sources be differing classes, differing antigen respones, or differing species of origin and whether or not the fusion point is at the variable/constant boundary. Thus, it is possible to produce antibodies in which neither the constant nor the variable region mimic known antibody sequences. It then becomes possible, for example, to construct antibodies whose variable region has a higher specific affinity for a particular antigen, or whose constant region can elicit enhanced complement fixation or to make other improvements in properties possessed by a particular constant region.

"Altered antibodies" means antibodies wherein the amino acid sequence has been varied from that of a mammalian or other vertebrate antibody. Because of the relevance of recombinant DNA techniques to this invention, one need not be confined to the sequences of amino acids found in natural antibodies; antibodies can be redesigned to obtain desired characteristics. The possible variations are many and range from the changing of just one or a few amino acids to the complete redesign of, for example, the constant region. Changes in the constant region will, in general, be made in order to improve the cellular process characteristics, such as complement fixation, interaction with membranes, and other effector functions. Changes in the variable region will be made in order to improve the antigen binding characteristics. The antibody can also be engineered so as to aid the specific delivery of a toxic agent according to the "magic bullet" concept. Alterations, can be made by standard recombinant techniques and also by oligonucleotide-directed mutagenesis techniques (Dalbadie-McFarland, et al *Proc. Natl. Acad. Sci.(USA)*, 79:6409 (1982)).

"Univalent antibodies" refers to aggregations which comprise a heavy chain/light chain dimer bound to the Fc (or stem) region of a second heavy chain. Such antibodies are specific for antigen, but have the additional desirable property of targeting tissues with specific antigenic surfaces, without causing its antigenic effectiveness to be impaired—i.e., there is no antigenic modulation. This phenomenon and the property of univalent antibodies in this regard is set forth in Glennie, M. J., et al., *Nature*, 295: 712 (1982). Univalent antibodies have heretofore been formed by proteolysis.

"Fab" region refers to those portions of the chains which are roughly equivalent, or analogous, to the sequences which comprise the Y branch portions of the heavy chain and to the light chain in its entirety, and which collectively (in aggregates) have been shown to exhibit antibody activity. "Fab protein", which protein is one of the aspects of the invention, includes aggregates of one heavy and one light chain (commonly known as Fab'), as well as tetramers which correspond to the two branch segments of the antibody Y, (commonly known as $F(ab)_2$), whether any of the above are covalently or non-covalently aggregated, so long as the aggregation is capable of selectively reacting with a particular antigen or antigen family. Fab antibodies have, as have univalent ones, been formed heretofore by proteolysis, and share the property of not eliciting antigen modulation on target tissues. However, as they lack the "effector" Fc portion they cannot effect, for example, lysis of the target cell by macrophages.

"Fab protein" has similar subsets according to the definition of the present invention as does the general term "antibodies" or "immunoglobulins". Thus, "mammalian" Fab protein, "hybrid" Fab protein "chimeric" Fab and "altered" Fab protein are defined analogously to the corresponding definitions set forth in the previous paragraphs for the various types of antibodies.

Individual heavy or light chains may of course be "mammalian", "chimeric" or "altered" in accordance with the above. As will become apparent from the detailed description of the invention, it is possible, using the techniques disclosed to prepare other combinations of the four-peptide chain aggregates, besides those specifically defined, such as hybrid antibodies containing chimeric light and mammalian heavy chains, hybrid Fab proteins containing chimeric Fab proteins of heavy chains associated with mammalian light chains, and so forth.

"Expression vector" includes vectors which are capable of expressing DNA sequences contained therein, i.e., the coding sequences are operably linked to other sequences capable of effecting their expression. It is implied, although not always explicitly stated, that these expression vectors must be replicable in the host organisms either as episomes or as an integral part of the chromosomal DNA. Clearly a lack of replicability would render them effectively inoperable. A useful, but not a necessary, element of an effective expression vector is a marker encoding sequence—i.e. a sequence encoding a protein which results in a phenotypic property (e.g. tetracycline resistance) of the cells containing the protein which permits those cells to be readily identified. In sum, "expression vector" is given a functional definition, and any DNA sequence which is capable of effecting expression of a specified contained DNA code is included in this term, as it is applied to the specified sequence. As at present, such vectors are frequently in the form of plasmids, thus "plasmid" and "expression vector" are often used interchangeably. However, the invention is intended to include such other forms of expression vectors which serve equivalent functions and which may, from time to time become known in the art.

"Recombinant host cells" refers to cells which have been transformed with vectors constructed using recombinant DNA techniques. As defined herein, the antibody or modification thereof produced by a recombinant host cell is by virtue of this transformation, rather than in such lesser amounts, or more commonly, in such less than detectable amounts, as would be produced by the untransformed host.

In descriptions of processes for isolation of antibodies from recombinant hosts, the terms "cell" and "cell culture" are used interchangeably to denote the source of antibody unless it is clearly specified otherwise. In other words, recovery of antibody from the "cells" may mean either from spun down whole cells, or from the cell culture containing both the medium and the suspended cells.

B. Host Cell Cultures and Vectors

The vectors and methods disclosed herein are suitable for use in host cells over a wide range of prokaryotic and eukaryotic organisms.

In general, of course, prokaryotes are preferred for cloning of DNA sequences in constructing the vectors useful in the invention. For example, *E. coli* K12 strain

294 (ATCC No. 31446) is particularly useful. Other microbial strains which may be used include *E. coli* strains such as *E. coli* B, and *E. coli* X1776 (ATTC No. 31537). These examples are, of course, intended to be illustrative rather than limiting.

Prokaryotes may also be used for expression. The aforementioned strains, as well as *E. coli* W3110 ($F^{31}$, $\lambda^-$, prototrophic, ATTC No. 27325), bacilli such as *Bacillus subtilus*, and other enterobacteriaceae such as *Salmonella typhimurium* or *Serratia marcesans*, and various *Pseudomonas* species may be used.

In general, plasmid vectors containing replicon and control sequences which are derived from species compatible with the host cell are used in connection with these hosts. The vector ordinarily carries a replication site, as well as marking sequences which are capable of providing phenotypic selection in transformed cells. For example, *E. coli* is typically transformed using pBR322, a plasmid derived from an *E. coli* species (Bolivar, et al., *Gene* 2: 95 (1977)). pBR322 contains genes for ampicillin and tetracycline resistance and thus provides easy means for identifying transformed cells. The pBR322 plasmid, or other microbial plasmid must also contain, or be modified to contain, promoters which can be used by the microbial organism for expression of its own proteins. Those promoters most commonly used in recombinant DNA construction include the β-lactamase (penicillinase) and lactose promoter systems (Chang et al, *Nature*, 275: 615 (1978); Itakura, et al, *Science*, 198: 1056 (1977); (Goeddel, et al *Nature* 281: 544 (1979)) and a tryptophan (trp) promoter system (Goeddel, et al, *Nucleic Acids Res.*, 8: 4057 (1980); EPO Appl Publ No. 0036776). While these are the most commonly used, other microbial promoters have been discovered and utilized, and details concerning their nucleotide sequences have been published, enabling a skilled worker to ligate them functionally with plasmid vectors (Siebenlist, et al, *Cell* 20: 269 (1980)).

In addition to prokaryates, eukaryotic microbes, such as yeast cultures may also be used. *Saccharomyces cerevisiae*, or common baker's yeast is the most commonly used among eukaryotic microorganisms, although a number of other strains are commonly available. For expression in Saccharomyces, the plasmid YRp7, for example, (Stinchcomb, et al, *Nature*, 282: 39 (1979); Kingsman et al, *Gene*, 7: 141 (1979); Tschemper, et al, *Gene*, 10: 157 (1980)) is commonly used. This plasmid already contains the trpl gene which provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example ATCC No. 44076 or PEP4-1 (Jones, *Genetics*, 85: 12 (1977)). The presence of the trpl lesion as a characteristic of the yeast host cell genome then provides an effective environment for detecting transformation by growth in the absence of tryptophan.

Suitable promoting sequences in yeast vectors include the promoters for 3-phosphoglycerate kinase (Hitzeman, et al., *J. Biol. Chem.*, 255: 2073 (1980)) or other glycolytic enzymes (Hess, et al, *J. Adv. Enzyme Reg.*, 7: 149 (1968); Holland, et al, *Biochemistry*, 17: 4900 (1978)), such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase. In constructing suitable expression plasmids, the termination sequences associated with these genes are also ligated into the expression vector 3' of the sequence desired to be expressed to provide polyadenylation of the mRNA and termination. Other promoters, which have the additional advantage of transcription controlled by growth conditions are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, and the aforementioned glyceraldehyde-3-phosphate dehydrogenase, an enzymes responsible for maltose and galactose utilization (Holland, ibid.). Any plasmid vector containing yeast-compatible promoter, origin of replication and termination sequences is suitable.

In addition to microorganisms, cultures of cells derived from multicellular organisms may also be used as hosts. In principle, any such cell culture is workable, whether from vertebrate or invertebrate culture. However interest has been greatest in vertebrate cells, and propogation of vertebrate cells in culture (tissue culture) has become a routine procedure in recent years (*Tissue Culture*, Academic Pres, Kruse and Patterson, editors (1973)). Examlples of such useful host cell lines are VERO and HeLa cells, Chinese hamster ovary (CHO) cell lines, and W138, BHK, COS-7 and MDCK cell lines. Expression vectors for such cells ordinarily include (if necessary) an origin of replication, a promoter located in front of the gene to be expressed, along with any necessary ribosome binding sites, RNA splice sites, polyadenylation site, and transcriptional terminator sequences.

For use in mammalian cells, the control functions on the expression vectors are often provided by viral material. For example, commonly used promoters are derived from polyoma, Adenovirus 2, and most frequently Simian Virus 40 (SV40). The early and late promoters of SV40 virus are particularly useful because both are obtained easily from the virus as a fragment which also contains the SV40 viral origin of replication (Fiers, et al, *Nature*, 273: 113 (1978)) incorporated herein by reference. Smaller or larger SV40 fragments may also be used, provided there is included the approximately 250 bp sequence extending from the Hind III site toward the Bgl I site located in the viral origin of replication. Further, it is also possible, and often desirable, to utilize promoter or control sequences normally associated with the desired gene sequence, provided such control sequences are compatible with the host cell systems.

An origin of replication may be provided either by construction of the vector to include an exogenous origin, such as may be derived from SV40 or other viral (e.g. Polyoma, Adeno, VSV, BPV, etc.) source, or may be provided by the host cell chromosomal replication mechanism. If the vector is integrated into the host cell chromosome, the latter is often sufficient.

It will be understood that this invention, although described herein in terms of a preferred embodiment, should not be construed as limited to those host cells, vectors and expression systems exemplified.

C. Methods Employed

C.1 Transformation

If cells without formidable cell wall barriers are used as host cells, transfection is carried out by the calcium phosphate precipitation method as described by Graham and Van der Eb, *Virology*, 52: 546 (1978). However, other methods for introducing DNA into cells such as by nuclear injection or by protoplast fusion may also be used.

If prokaryotic cells or cells which contain substantial cell wall constructions are used, the preferred method

of transfection is calcium treatment using calcium chloride as described by Cohen, F. N. et al *Proc. Natl. Acad. Sci. (USA)*, 69: 2110 (1972).

C.2 Vector Construction

Construction of suitable vectors containing the desired coding and control sequences employ standard ligation techniques. Isolated plasmids or DNA fragments are cleaved, tailored, and religated in the form desired to form the plasmids required. The methods employed are not dependent on the DNA source, or intended host.

Cleavage is performed by treating with restriction enzyme (or enzymes) in suitable buffer. In general, about 1 μg plasmid or DNA fragments is used with about 1 unit of enzyme in about 20 μl of buffer solution. (Appropriate buffers and substrate amounts for particular restriction enzymes are specified by the manufacturer.) Incubation times of about 1 hour at 37° C. are workable. After incubations, protein is removed by extraction with phenol and chloroform, and the nucleic acid is recovered from the aqueous fraction by precipitation with ethanol.

If blunt ends are required, the preparation is treated for 15 minutes at 15° with 10 units of *E. coli* DNA Polymerase I (Klenow), phenol-chloroform extracted, and ethanol precipitated.

Size separation of the cleaved fragments is performed using 6 percent polyacrylamide gel described by Goeddel, D., et al, *Nucleic Acids Res.*, 8: 4057 (1980) incorporated herein by reference.

For ligation, approximately equimolor amounts of the desired components, suitably end tailored to provide correct matching are treated with about 10 units T4 DNA ligase per 0.5 μg DNA. (When cleaved vectors are used as components, it may be useful to prevent religation of the cleaved vector by pretreatment with bacterial alkaline phosphatase.)

In the examples described below correct ligations for plasmid construction are confirmed by transforming *E. coli* K12 strain 294 (ATCC 31446) with the ligation mixture. Successful transformants were selected by ampicillin or tetracycline resistance depending on the mode of plasmid construction. Plasmids from the transformants were then prepared, analyzed by restriction and/or sequenced by the method of Messing, et al, *Nucleic Acids Res.*, 9: 309 (1981) or by the method of Maxam, et al, *Methods in Enzymology*, 65: 499 (1980).

D. Outline of Procedures

D.1 Mammalian Antibodies

The first type of antibody which forms a part of this invention, and is prepared by the methods thereof, is "mammalian antibody"-one wherein the heavy and light chains mimic the amino acid sequences of an antibody otherwise produced by a mature mammalian B lymphocyte either in situ or when fused with an immortalized cell as part of a hybridoma culture. In outline, these antibodies are produced as follows:

Messenger RNA coding for heavy or light chain is isolated from a suitable source, either mature B cells or a hybridoma culture, employing standard techniques of RNA isolation, and the use of oligo-dT cellulose chromatography to segregate the poly-A mRNA.. The poly-A mRNA may, further, be fractionated to obtain sequences of sufficient size to code for the amino acid sequences in the light or heavy chain of the desired antibody as the case may be.

A cDNA library is then prepared from the mixture of mRNA using a suitable primer, preferably a nucleic acid sequence which is characteristic of the desired cDNA. Such a primer may be hypothesized and synthesized based on the amino acid sequence of the antibody if the sequence is known. In the alternative cDNA from unfractionated poly-A mRNA from a cell line producing the desired antibody or poly-dT may also be used. The resulting cDNA is optionally size fractionated on polyacrylamide gel and then extended with, for example, dC residues for annealing with pBR322 or other suitable cloning vector which has been cleaved by a suitable restriction enzyme, such as Pst I, and extended with dG residues. Alternative means of forming cloning vectors containing the cDNA using other tails and other cloning vector remainder may, of course, also be used but the foregoing is a standard and preferable choice. A suitable host cell strain, typically *E. coli*, is transformed with the annealed cloning vectors, and the successful transformants identified by means of, for example, tetracycline resistance or other phenotypic characteristic residing on the cloning vector plasmid.

Successful transformants are picked and transferred to microtiter dishes or other support for further growth and preservation. Nitrocellulose filter imprints of these growing cultures are then probed with suitable nucleotide sequences containing bases known to be complementary to desired sequences in the cDNA. Several types of probe may be used, preferably synthetic single stranded DNA sequences labeled by kinasing with $ATP^{32}$. The cells fixed to the nitrocellulose filter are lysed, the DNA denatured, and then fixed before reaction with kinased probe. Clones which successfully hybridize are detected by contact with a photoplate, then plasmids from the growing colonies isolated and sequenced by means known in the art to verify that the desired portions of the gene are present.

The desired gene fragments are excised and tailored to assure appropriate reading frame with the control segments when inserted into suitable expression vectors. Typically, nucleotides are added to the 5' end to include a start signal and a suitably positioned restriction endonuclease site.

The tailored gene sequence is then positioned in a vector which contains a promoter in reading frame with the gene and compatible with the proposed host cell. A number of plasmids such as those described in U.S. Pat. Nos. 4,663,283 and 4,456,748 and pending U.S. Ser. No. 291,892, have been described which already contain the appropriate promoters, control sequences, ribosome binding sites, and transcription termination sites, as well as convenient markers.

In the present invention, the gene coding for the light chain and that coding for the heavy chain are recovered separately by the procedures outlined above. Thus they may be inserted into separate expression plasmids, or together in the same plasmid, so long as each is under suitable promoter and translation control.

The expression vectors constructed above are then used to transform suitable cells. The light and heavy chains may be transformed into separate cell cultures, either of the same or of differing species; separate plasmids for light and heavy chain may be used to co-transform a single cell culture, or, finally, a single expression plasmid containing both genes and capable of expressing the genes for both light and heavy chain may be transformed into a single cell culture.

Regardless of which of the three foregoing options is chosen, the cells are grown under conditions appropriate to the production of the desired protein. Such condi-

tions are primarily mandated by the type of promoter and control systems used in the expression vector, rather than by the nature of the desired protein. The protein thus produced is then recovered from the cell culture by methods known in the art, but choice of which is necessarily dependent on the form in which the protein is expressed. For example, it is common for mature heterologous proteins expressed in *E. coli* to be deposited within the cells as insoluble particles which require cell lysis and solubilization in denaturant to permit recovery. On the other hand, proteins under proper synthesis circmstances, in yeast and bacterial strains, can be secreted into the medium (yeast and gram positive bacteria) or into the periplasmic space (gram negative bacteria) allowing recovery by less drastic procedures. Tissue culture cells as hosts also appear, in general, to permit reasonably facile recovery of heterologous proteins.

When heavy and light chain are coexpressed in the same host, the isolation procedure is designed so as to recover reconstituted antibody. This can be accomplished in vitro as described below, or might be possible in vivo in a microorganism which secretes the IgG chains out of the reducing environment of the cytoplasm. A more detailed description is given in D.2, below.

D.2 Chain Recombination Techniques

The ability of the method of the invention to produce heavy and light chains or portions thereof, in isolation from each other offers the opportunity to obtain unique and unprecedented assemblies of immunoglobulins, Fab regions, and univalent antibodies. Such preparations require the use of techniques to reassemble isolated chains. Such means are known in the art, and it is, thus, appropriate to review them here.

While single chain disulfide bond containing proteins have been reduced and reoxidized to regenerate in high yield native structure and activity (Freedman, R. B., et al. In *Enzymology of Post Translational Modification of Proteins*, I: 157-212 (1980) Academic Press, NY.), proteins which consist of discontinuous polypeptide chains held together by disulfide bonds are more difficult to reconstruct in vitro after reductive cleavage. Insulin, a cameo case, has received much experimental attention over the years, and can now be reconstructed so efficiently that an industrial process has been built around it (Chance, R. E., et al., In *Peptides: Proceedings of the Seventh Annual American Peptide Symposium* (Rich, D. H. and Gross, E., eds.) 721-728, Pierce Chemical Co., Rockford, IL. (1981)).

Immunoglobulin has proved a more difficult problem than insulin. The tetramer is stabilized intra and intermolecularly by 15 or more disulfide bonds. It has been possible to recombine heavy and light chains, disrupted by cleavage of only the interchain disulfides, to regain antibody activity even without restoration of the interchain disulfides (Edelman, G. M., et al., *Proc. Natl. Acad. Sci (USA)* 50: 753 (1963)). In addition, active fragments of IgG formed by proteolysis (Fab fragments of ~50,000 MW) can be split into their fully reduced heavy chain and light chain components and fairly efficiently reconstructed to give active antibody (Haber, E., *Proc. Natl. Acad. Sci. (USA)* 52: 1099 (1964); Whitney, P. L., et al., *Proc. Natl. Acad. Sci. (USA)* 53: 524 (1965)). Attempts to reconstitute active antibody from fully reduced native IgG have been largely unsuccessful, presumably due to insolubility of the reduced chains and of side products or intermediates in the refolding pathway (see discussion in Freedman, M. H., et al., *J. Biol. Chem.* 241: 5225 (1966)). If, however, the immunoglobulin is randomly modified by polyalanylation of its lysines before complete reduction, the separated chains have the ability to recover antigen-combining activity upon reoxidation (ibid).

A particularly suitable method for immunoglobulin reconstitution is derivable from the now classical insulin recombination studies, wherein starting material was prepared by oxidative sulfitolysis, thus generating thiol-labile S-sulfonate groups at all cysteines in the protein, non-reductively breaking disulfides (Chance et al. (supra)). Oxidative sulfitolysis is a mild disulfide cleavage reaction (Means, G. E., et al., *Chemical Modification of Proteins*, Holden-Day, San Francisco (1971) which is sometimes more gentle than reduction (Wetzel, R., *Biochemistry*, submitted (1983)), and which generates derivatives which are stable until exposed to mild reducing agent at which time disulfide reformation can occur via thiol-disulfide interchange (Morehead, H., et al. *Biochemistry*, in press, (1983)). In the present invention the heavy and light chain S-sulfonates generated by oxidative sulfitolysis were reconstituted utilizing both air oxidation and thiol-disulfide interchange to drive disulfide bond formation. The general procedure is set forth in detail in U.S. Pat. No. 4,599,197 incorporated herein by reference.

D.3 Variants Permitted by Recombinant Technology

Using the techniques described in paragraphs D.1 and D.2, additional operations which were utilized to gain efficient production of mammalian antibody can be varied in quite straightforward and simple ways to produce a great variety of modifications of this basic antibody form. These variations are inherent in the use of recombinant technology, which permits modification at a genetic level of amino acid sequences in normally encountered mammalian immunoglobulin chains, and the great power of this approach lies in its ability to achieve these variations, as well as in its potential for economic and specific production of desired scarce, and often contaminated, molecules. The variations also inhere in the ability to isolate production of individual chains, and thus create novel assemblies.

Briefly, since genetic manipulations permit reconstruction of genomic material in the process of construction of expression vectors, such reconstruction can be manipulated to produce new coding sequences for the components of "natural" antibodies or immunoglobulins. As discussed in further detail below, the coding sequence for a mammalian heavy chain may not be derived entirely from a single source or a single species, but portions of a sequence can be recovered by the techniques described in D.1 from differing pools of mRNA, such as murine-murine hybridomas, human-murine hybridomas, or B cells differentiated in response to a series of antigen challenges. The desired portions of the sequences in each case can be recovered using the probe and analysis techniques described in D.1, and recombined in an expression vector using the same ligation procedures as would be employed for portions of the same model sequence. Such chimeric chains can be constructed of any desired length; hence, for example, a complete heavy chain can be constructed, or only sequence for the Fab region thereof.

The additional area of flexibility which arises from the use of recombinant techniques results from the power to produce heavy and light chains or fragments thereof in separate cultures or of unique combinations

of heavy and light chain in the same culture, and to prevent reconstitution of the antibody or immunoglobulin aggregation until the suitable components are assembled. Thus, while normal antibody production results automatically in the formation of "mammalian antibodies" because the light and heavy chain portions are constructed in response to a particular determinant in the same cell, the methods of the present invention present the opportunity to assemble entirely new mixtures. Somewhat limited quantities of "hybrid" antibodies have been produced by "quadromas" i.e., fusions of two hybridoma cell cultures which permit random assemblies of the heavy and light chains so produced.

The present invention permits a more controlled assembly of desired chains, either by mixing the desired chains in vitro, or by transforming the same culture with the coding sequences for the desired chains.

D.4 Composite Immunoglobulins

The foregoing procedure, which describes in detail the recombinant production of mammalian antibodies is employed with some modifications to construct the remaining types of antibodies or NSIs encompassed by the present invention. To prepare the particular embodiment of composite non-specific immunoglobulin wherein the homology of the chains corresponds to the sequences of immunoglobulins of different specificities, it is of course, only necessary to prepare the heavy and light chains in separate cultures and reassemble them as desired.

For example, in order to make an anti-CEA light chain/anti-hepatitis heavy chain composite antibody, a suitable source for the mRNA used as a template for the light chain clone would comprise, for instance, the anti CEA producing cell line of paragraph E.1. The mRNA corresponding to heavy chain would be derived from B cells raised in response to hepatitis infection or from hybridoma in which the B cell was of this origin. It is clear that such composites can be assembled using the methods of the invention almost at will, and are limited only by available sources of mRNA suitable for use as templates for the respective chains. All other features of the process are similar to those described above.

D.5 Hybrid Antibodies

Hybrid antibodies are particularly useful as they are capable of simultaneous reaction with more than one antigen. Pairs of heavy and light chains corresponding to chains of antibodies for different antigens, such as those set forth in paragraph D.4 are prepared in four separate cultures, thus preventing premature assembly of the tetramer. Subsequent mixing of the four separately prepared peptides then permits assembly into the desired tetramers. While random aggregation may lead to the formation of considerable undesired product, that portion of the product in which homologous light and heavy chains are bound to each other and mismatched to another pair gives the desired hybrid antibody.

D.6 Chimeric Antibodies

For construction of chimeric antibodies (wherein, for example, the variable sequences are separately derived from the constant sequences) the procedures of paragraph D.1 and D.2 are again applicable with appropriate additions and modifications. A preferred procedure is to recover desired portions of the genes encoding for parts of the heavy and light chains from suitable, differing, sources and then to religate these fragments using restriction endonucleases to reconstruct the gene coding for each chain.

For example, in a particular preferred chimeric construction, portions of the heavy chain gene and of the light chain gene which encode the variable sequences of antibodies produced by a murine hybridoma culture are recovered and cloned from this culture and gene fragments encoding the constant regions of the heavy and light chains for human antibodies recovered and cloned from, for example, human myeloma cells. Suitable restriction enzymes may then be used to ligate the variable portions of the mouse gene to the constant regions of the human gene for each of the two chains. The chimeric chains are produced as set forth in D.1, aggregated as set forth in D.2 and used in the same manner as the non-chimeric forms. Of course, any splice point in the chains can be chosen.

D.7 Altered Antibodies

Altered antibodies present, in essence, an extension of chimeric ones. Again, the techniques of D.1 and D.2 are applicable; however, rather than splicing portions of the chain(s), suitable amino acid alterations, deletions or additions are made using available techniques such as mutagenesis (supra). For example, genes which encode antibodies having diminished complement fixation properties, or which have enhanced metal binding capacities are prepared using such techniques. The latter type may, for example, take advantage of the known gene sequence encoding metalothionein II (Karin, M., et al., *Nature*, 299: 797 (1982)). The chelating properties of this molecular fragment are useful in carrying heavy metals to tumor sites as an aid in tumor imaging (Scheinberg, D. A., et al., *Science*, 215: 19 (1982).

D.8 Univalent Antibodies

In another preferred embodiment, antibodies are formed which comprise one heavy and light chain pair coupled with the Fc region of a third (heavy) chain. These antibodies have a particularly useful property. They can, like ordinary antibodies, be used to target antigenic surfaces of tissues, such as tumors, but, unlike ordinary antibodies, they do not cause the antigenic surfaces of the target tissue to retreat and become non-receptive. Ordinary antibody use results in aggregation and subsequent inactivation, for several hours, of such surface antigens.

The method of construction of univalent antibodies is a straightforward application of the invention. The gene for heavy chain of the desired Fc region is cleaved by restriction enzymes, and only that portion coding for the desired Fc region expressed. This portion is then bound using the technique of D.2 to separately produced heavy chain the desired pairs separated from heavy/heavy and Fc/Fc combinations, and separately produced light chain added. Pre-binding of the two heavy chain portions thus diminishes the probability of formaion of ordinary antibody.

D.9 Fab Protein

Similarly, it is not necessary to include the entire gene for the heavy chain portion. All of the aforementioned variations can be superimposed on a procedure for Fab protein production and the overall procedure differs only in that that portion of the heavy chain coding for the amino terminal 220 amino acids is employed in the appropriate expression vector.

E. Specific Examples of Preferred Embodiments

The invention has been described above in general terms and there follow several specific examples of embodiments which set forth details of experimental procedure in producing the desired antibodies. Example E.1 sets forth the general procedure for preparing anti

CEA antibody components, i.e. for a "mammalian antibody". Example E.3 sets forth the procedure for reconstitution and thus is applicable to preparation of mammalian, composite, hybrid and chimeric immunoglobulins, and Fab proteins and univalent antibodies. Example E.4 sets forth the procedure for tailoring the heavy or light chain so that the variable and constant regions may be derived from different sources. Example E.5 sets forth the method of obtaining a shortened heavy chain genome which permits the production of the Fab regions and, in an analogous manner, Fc region.

The examples set forth below are included for illustrative purposes and do not limit the scope of the invention.

E.1 Construction of Expression Vectors for Murine anti-CEA Antibody Chains and Peptide Synthesis

Carcinoembryonic antigen (CEA) is associated with the surface of certain tumor cells of human origin (Gold, P., et al., *J. Exp. Med.*, 122: 467 (1965)). Antibodies which bind to CEA (anti-CEA antibodies) are useful in early detection of these tumors (Van Nagell, T. R., et al., *Cancer Res.* 40: 502 (1980)), and have the potential for use in treatment of those human tumors which appear to support CEA at their surfaces. A mouse hybridoma cell line which secretes anti-CEA antibodies of the $Ig\gamma_1$ class, CEA.66-E3, has been prepared as described by Wagener, C, et al., *J. Immunol.* (in press) which is incorporated herein by reference, and was used as mRNA source. The production of anti CEA antibodies by this cell line was determined. The N-terminal sequences of the antibodies produced by these cells was compared with those of monoclonal anti CEA as follows. Purified IgG was treated with PCAse (Podell, D. N., et al., BBRC 81: 176 (1978)), and then dissociated in 6M guanidine hydrochloride, 10 mM 2-mercaptoethanol (1.0 mg of immunoglobulin, 5 min, 100° C. water bath). The dissociated chains were separated on a Waters Associates alkyl phenyl column using a liner gradient from 100 percent A (0.1 percent TFA-water) to 90 percent B (TFA/$H_2O$/MeCN 0.1/9.9/90) at a flow rate of 0.8 ml/min. Three major peaks were eluted and analyzed on SDS gels by silver staining. The first two peaks were pure light chain (MW 25,000 daltons), the third peak showed a (7:3) mixture of heavy and light chain. 1.2 nmoles of light chain were sequenced by the method of Shively, J. E., *Methods in Enzymology*, 79: 31 (1981), with an $NH_2$-terminal yield of 0.4 nmoles. A mixture of heavy and light chains (3 nmoles) was also sequenced, and sequence of light chain was deducted from the double sequence to yield the sequence of the heavy chain.

In the description which follows, isolation and expression of the genes for the heavy and light chains for anti CEA antibody produced by CEA.66-E3 are described. As the constant regions of these chains belong to the gamma and kappa families, respectively, "light chain" and "kappa chain", and "heavy chain" and "gamma chain", respectively, are used interchangeably below.

E.1.1 Isolation of Messenger RNA for Anti CEA Light and Heavy (Kappa and Gamma) Chains

Total RNA for CEA.66-E3 cells was extracted essentially as reported by Lynch et al, *Virology*, 98: 251 (1979). Cells were pelleted by centrifugation and approximately 1 g portions of pellet resuspended in 10 ml of 10 mM NaCl, 10 mM Tris HCl (pH 7.4), 1.5 mM $MgCl_2$. The resuspended cells were lysed by addition of non-ionic detergent NP-40 to a final concentration of 1 percent, and nuclei removed by centrifugation. After addition of SDS (pH 7.4) to 1 percent final concentration, the supernatant was extracted twice with 3 ml portions of phenol (redistilled)/chloroform:isoamyl alcohol 25:1 at 4° C. The aqueous phase was made 0.2M in NaCl and total RNA was precipitated by addition of two volumes of 100 percent ethanol and overnight storage at −20° C. After centrifugation, polyA mRNA was purified from total RNA by oligo-dT cellulose chromatography as described by Aviv and Leder, *Proc. Nat'l. Acad. Sci (USA)*, 69: 1408 (1972). 142 μg of polyA mRNA was obtained from 1 g cells.

E.1.2 Preparation of *E. coli* Colony Library Containing Plasmids with Heavy and Light DNA Sequence Inserts

5 μg of the unfractionated polyA mRNA prepared in paragraph E.1.1 was used as template for oligo-dT primed preparation of double-stranded (ds) cDNA by standard procedures as described by Goeddel et al., Nature 281: 544 (1979) and Wickens et al., *J. Biol. Chem.* 253: 2483 (1978) incorporated herein by reference. The cDNA was size fractionated by 6 percent polyacrylamide gel electrophoresis and 124 ng of ds cDNA greater than 600 base pairs in length was recovered by electroelution. A 20 ng portion of ds cDNA was extended with deoxy C residues using terminal deoxynucleotidyl transferase as described in Chang et al., *Nature* 275: 617 (1978) incorporated herein by reference, and annealed with 200 ng of the plasmid pBR322 (Bolivar et al., *Gene* 2: 95 (1977)) which had been cleaved with Pst I and tailed with deoxy G. Each annealed mixture was then transformed into *E. coli* K12 strain 294 (ATCC No. 31446). Approximately 8500 ampicillin sensitive, tetracycline resistant transformants were obtained.

E.1.3 Preparation of Synthetic Probes

The 14 mer, 5'GGTGGGAAGATGGA 3' complementary to the coding sequence of constant region for mous MOPC21 kappa chain which begins 25 basepairs 3' of the variable region DNA sequence was used as kappa chain probe. A 15 mer, 5'GACCAGGCATCCCAG 3', complementary to a coding sequence located 72 basepairs 3' of the variable region DNA sequence for mouse MOPC21 gamma chain was used to probe gamma chain gene.

Both probes were synthesized by the phosphotriester method described in German Offenlegungschrift No. 2644432, incorporated herein by reference, and made radioactive by kinasing as follows: 250 ng of deoxyoligonucleotide were combined in 25 μl of 60 mM Tris HCl (pH 8), 10 mM $MgCl_2$, 15 mM beta-mercaptoethanol, and 100 μCi ($\gamma$-$^{32}$P) ATP (Amersham, 5000 Ci/mMole). 5 units of T4 polynucleotide kinase were added and the reaction was allowed to proceed at 37° C. for 30 minutes and terminated by additon of EDTA to 20 mM.

E.1.4 Screening of Colony Library for Kappa or Gamma Chain Sequences

~2000 colonies prepared as described in paragraph E.1.2 were individually inoculated into wells of microtitre dishes containing LB (Miller, Experiments in Molecular Genetics, p. 431-3, Cold Spring Harbor Lab., Cold Spring Harbor, N.Y. (1972))+5 μg/ml tetracycline and stored at −20° C. after addition of DMSO to 7 percent. Individual colonies from this library were transferred to duplicate sets of Schleicher and Schuell BA85/20 nitrocellulose filters and grown on agar plates containing LB+5 μg/ml tetracycline. After ~10 hours growth at 37° C. the colony filters

were transferred to agar plates containing LB+5 μg/ml tetracycline and 12.5 μg/ml chloramphicol and reincubated overnight at 37° C. The DNA from each colony was then denatured and fixed to the filter by a modification of the Grunstein-Hogness procedure as described in Grunstein et al., *Proc. Natl. Acad. Sci. (USA)* 72: 3961 (1975), incorporated herein by reference. Each filter was floated for 3 minutes on 0.5N NaOH, 1.5M NaCl to lyse the colonies and denature the DNA then neutralized by floating for 15 minutes on 3M NaCl, 0.5M Tris HCl (pH 7.5). The filters were then floated for an additional 15 minutes on 2×SSC, and subsequently baked for 2 hours in an 80° C. vacuum oven. The filters were prehybridized for ~2 hours at room temperature in 0.9M NaCl, 1× Denhardts, 100 mM Tris HCl (pH 7.5), 5 mM Na-EDTA, 1 mM ATP, 1M sodium phosphate (dibasic), 1 mM sodium pyrophosphate, 0.5 percent NP-40, and 200 μg/ml *E. coli* t-RNA, and hybridized in the same solution overnight, essentially as described by Wallace et al. *Nucleic Acids Research* 9: 879 (1981) using ~$40\times10^6$ cpm of either the kinased kappa or gamma probe described above.

After extensive washing at 37° C. in 6X SSC, 0.1 percent SDS, the filters were exposed to Kodak XR-5 X-ray film with DuPont Lightning-Plus intensifying screens from 16–24 hours at −80° C. Approximately 20 colonies which hybridized with kappa chain probe and 20 which hybridized with gamma chain probe were characterized.

E.1.5 Characterization of Colonies which Hybridize to Kappa DNA Sequence Probe

Plasmid DNAs isolated from several different transformants which hybridized to kappa chain probe were cleaved with Pst I and fractionated by polyacrylamide gel electrophoresis (PAGE). This analysis demonstrated that a number of plasmid DNAs contained cDNA inserts large enough to encode full length kappa chain. The complete nucleotide sequence of the cDNA insert of one of these plasmids was determined by the dideoxynucleotide chain termination method as described by Smith, *Methods Enzymol.* 65, 560 (1980) incorporated herein by reference after subcloning restriction endonuclease cleavage fragments into M13 vectors (Messing et al., *Nucleic Acids Research* 9: 309 (1981). FIG. 2 shows the nucleotide sequence of the cDNA insert of pK17G4 and FIG. 3 shows the gene sequence with the corresponding amino acid sequence. Thus, the entire coding region of mouse anti-CEA kappa chain was isolated on this one large DNA fragment. The amino acid sequence of kappa chain, deduced from the nucleotide sequence of the pK17G4 cDNA insert, corresponds perfectly with the first 23 N-terminal amino acids of mature mouse anti-CEA kappa chain as determined by amino acid sequence analysis of purified mouse anti-CEA kappa chain. The coding region of pK17G4 contains 27 basepairs or 9 amino acids of the presequence and 642 basepairs or 214 amino acids of the mature protein. The mature unglycosylated protein (MW 24,553) has a variable region of 119 amino acids, including the J1 joining region of 12 amino acids, and a constant region of 107 amino acids. After the stop codon behind amino acid 215 begins 212 basepairs of 3' untranslated sequence up to the polyA addition. The kappa chain probe used to identify pK17G4 hybridizes to nucleotides 374–388 (FIG. 2).

E.1.6. Characterization of Colonies which Hybridize to Gamma 1 DNA Probe

Plasmid DNA isolated from several transformants positive for hybridization with the heavy chain gamma 1 probe was subjected to Pst I restriction endonuclease analysis as described in E.1.5. Plasmid DNAs demonstrating the largest cDNA insert fragments were selected for further study. Nucleotide sequence coding for mouse heavy (gamma-1) chain, shows an NcoI restriction endonuclease cleavage site near the junction between variable and constant region. Selected plasmid DNAs were digested with both PstI and NcoI and sized on polyacrylamide. This analysis allowed identification of a number of plasmid DNAs that contain NcoI restriction endonuclease sites, although none that demonstrate cDNA insert fragments large enough to encode the entire coding region of mouse anti-CEA heavy chain.

In one plasmid isolated, p γ298 the cDNA insert of about 1300 bp contains sequence information for the 5' untranslated region, the signal sequence and the N-terminal portion of heavy chain. Because pγ298 did not encode the C-terminal sequence for mouse anti-CEA gamma 1 chain, plasmid DNA was isolated from other colonies and screened with PstI and NcoI. The C-terminal region of the cDNA insert of pγ11 was sequenced and shown to contain the stop codon, 3' untranslated sequence and that portion of the coding sequence missing from p γ298.

FIG. 4 presents the entire nucleotide sequence of mouse anti-CEA heavy chain (as determined by the dideoxynucleotide chain termination method of Smith, *Methods Enzymol.*, 65: 560 (1980)) and FIG. 5 includes the translated sequence.

The amino acid sequence of gamma 1 (heavy chain) deduced from the nucleotide sequence of the pγ298 cDNA insert corresponds perfectly to the first 23 N-terminal amino acids of mature mouse anti-CEA gamma 1 chain as determined by amino acid sequence analysis of purified mouse anti-CEA gamma-1 chain. The coding region consists of 57 basepairs or 19 amino acids of presequences and 1346 basepairs or 447 amino acids of mature protein. The mature unglycosolated protein (MW 52,258) has a variable region of 135 amino acids, including a D region of 12 amino acids, and a J4 joining region of 13 amino acids. The constant region is 324 amino acids. After the stop codon behind amino acid 447 begins 96 bp of 3' untranslated sequences up to the polyA addition. The probe used to identify pγ298 and pγ11 hybridized to nucleotides 528–542 (FIG. 4).

E.1.7 Construction of a Plasmid For Direct Expression of Mouse Mature Anti-CEA Kappa Chain Gene, pKCEAtrp207-1*

FIG. 6 illustrates the construction of pKCEAtrp207-1*

First, an intermediate plasmid pHGH207-1*, having a single trp promoter, was prepared as follows:

The plasmid pHGH 207 (described in U.S. Pat. No. 4,663,283), was used to prepare pHGH 207-1, pHGH 207 was digested with BamHI, followed by partial digestion with EcoRI. The largest fragment, which contains the entire trp promoter, was isolated and ligated to the largest EcoRI-BamHI fragment from pBR322, and the ligation mixture used to transform *E. coli* 294. Tet and Amp resistant colonies were isolated, and most of them contained pHGH207-1. pHGH207-1* which lacks the EcoR1 site between the $amp^R$ gene and the trp promoter, was obtained by partial digestion of pHGH207-1 (de Boer et al., *Promoters*, Rodriquez et al. Eds. (1982), pp. 462–481 U.S. Pat. No. 4,663,283) with

EcoR I, filling in the ends with Klenow and dNTPs, and religation.

5 μg of pHGH207-1* was digested with EcoRI, and the ends extended to blunt ends using 12 units of DNA Polymerase I in a 50 μl reaction containing 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4) and 1 mM in each dNTP at 37° C. for 1 hour, followed; by extraction with phenol/$CHCl_3$ and precipitation with ethanol. The precipitated DNA was digested with BamH I, and the large vector fragment (fragment 1) purified using 5 percent polyacrylamide gel electrophoresis, electroelution, phenol/$CHCl_3$ extraction and ethanol precipitation.

The DNA was resuspended in 50 μl of 10 mM Tris pH 8, 1 mM EDTA and treated with 500 units Bacterial Alkaline Phosphatase (BAP) for 30' at 65° followed by phenol/$CHCl_3$ extraction and ethanol precipitation.

A DNA fragment containing part of the light chain sequence was prepared as follows: 7 μg of pK17G4 DNA was digested with Pst I and the kappa chain containing cDNA insert was isolted by 6 percent gel electrophoresis, and electroelution. After phenol/$CHCl_3$ extraction, ethanol precipitaion and resuspensionin water, this fragment was digested with Ava II. The 333 bp Pst I-Ava II DNA fragment was isolated and purified from a 6 percent polyacrylamide gel.

A 15 nucleotide DNA primer was synthesized by the phosphotriester method G.O. 2,644,432 (supra) and has the following sequence:

Met Asp Ile Val Met
5' ATG GAC ATT GTT ATG 3'

The 5' methionine serves as the initiation codon. 500 ng of this primer was phosphorylated at the 5' end with 10 units T4 DNA kinase in 20 μl reaction containing 0.5 mM ATP. ~200 ng of the Pst I-Ava II DNA fragment was mixed with the 20 μl of the phosphorylated primer, heated to 95° C. for 3 minutes and quick frozen in a dry-ice ethanol bath. The denatured DNA solution was made 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4), 12 mM in each dNTP and 12 units DNA Polymerase I-Large Fragment was added. After 2 hours incubation at 37° C. this primer repair reaction was phenol/$CHCl_3$ extracted, ethanol precipitated, and digested to completion with Sau 3A. The reaction mixture was then electrophoresed on a 6 percent polyacrylamide gel and ~50 ng of the 182 basepair amino-terminal blunt-end to Sau 3A fragment (fragment 2) was obtained after electroelution.

100 ng of fragment 1 (supra) and 50 ng of fragment 2 were combined in 20 μl of 20 mM Tris HCl (pH 7.5), 10 mM $MgCl_2$, 10 mM DTT, 2.5 mM ATP and 1 unit of T4 DNA ligase. After overnight ligation at 14° C. the reaction was transformed into *E. coli* K12 strain 294. Restriction endonuclease digestion of plasmid DNA from a number of ampicillin resistant transformants indicated the proper construction and DNA sequene analysis proved the desired nucleotide sequence through the initiation codon of this new plasmid, pKCEAInt1 (FIG. 6).

The remainder of the coding sequence of the kappa light chain gene was prepared as follows:

The Pst I cDNA insert fragment from 7 μg of K17G4 DNA was partially digested with Ava II and the Ava II cohesive ends were extended to blunt ends in a DNA Polymerase I large fragment reaction. Following 6 percent polyacrylamide gel electrophoresis the 686 basepair Pst I to blunt ended Ava II DNA fragment was isolated, purified and subjected to Hpa II restriction endonuclease digestion. The 497 basepair Hpa II to blunt ended Ava II DNA fragment (fragment 3) was isoated and purified after gel electrophoresis.

10 μg of pKCEAInt1 DNA was digested with Ava I, extended with DNA polymerase I large fragment, and digested with Xba I. Both the large blunt ended Ava I to Xba I vector fragment and the small blunt ended Ava I to Xba I fragment were isolated and purified from a 6 percent polyacrylamide gel after electrophoresis. The large vector fragment (fragment 4) was treated with Bacterial Alkaline Phosphatase (BAP), and the small fragment was digested with Hpa II, electrophoresed on a 6 percent polyacrylamide and the 169 basepair Xba I-Hpa II DNA fragment (fragment 5) was purified. ~75 ng of fragment 4, ~50 ng of fragment 3 and ~50 ng of fragment 5 were combined in a T4 DNA ligase reactin and incubated overnight at 14°, and the reaction mixture transformed into *E. coli* K12 strain 294. Plasmid DNA from six ampicillin resistant transformants were analyzed by restriction endonuclease digestion. One plasmid DNA demonstrated the proper construction and was digested pKCEAInt2.

Final construction was effected by ligating the K-CEA fragment, including the trp promoter from pKCEAInt2 into pBR322(XAP). (pBR322(XAP) is prepared by deletion of the region of pBR322 between its unique AvaI and PvaII sites)

The K-CEA fragment was prepared by treating pKCEAInt2 with Ava I, blunt ending with DNA polymerase I (Klenow fragment) in the presence of DNTPs, digestion with Pst I and isolation of the desired fragment by gel electrophoresis and electroelution.

The large vector fragment from pBR322(XAP) was prepared by successive treatment with EcoR I, blunt ending with polymerase, and redigestion with Pst I, followed by isolation of the large vector fragment by electrophoresis and electroelution.

The K-CEA and large vector fragments as prepared in the preceding paragraphs were ligated with T4 DNA ligase, and the ligation mixture transformed into *E. coli* as above. Plasmid DNA from several ampicillin resistant transformants were selected for analysis, and one plasmid DNA demonstrated the proper construction, and was designated pKCEAtrp207-1*.

E.1.8 Construction of a Plasmid Vector for Direct Expression of Mouse Mature Anti-CEA Heavy (Gamma 1) Chain Gene, pγCEAtrp207-1*

FIG. 7 illustrates the construction of pγCEAtrp207-1*. This plasmid was constructed in two parts beginning with construction of the C-terminal regin of the gamma 1 gene.

5 μg of plasmid pHGH207-1* was digested with Ava I, extended to blunt ends with DNA polymerase I large fragment (Klenow fragment), extracted with phenol/$CHCl_3$, and ethanol precipitated. The DNA was digested with BamH I treated with BAP and the large fragment (fragment A) was purified by 6 percent polyacrylamide gel electrophoresis and electroelution.

~5 μg of pγ11 was digested with Pst I and the gamma chain cDNA insert fragment containing the C-terminal portion of the gene was purified, digested with Ava II followed by extension of the Ava II cohesive ends with Klenow, followed by Taq I digestion. The 375 basepair blunt ended Ava II to Taq I fragment

(fragment B) was isolated and purified by gel electrophoresis and electroelution.

9 μg of pγ298 was digested with Taq I and BamH I for isolation of the 496 basepair fragment (fragment C).

Approximately equimolar amounts of fragments A, B, and C were ligated overnight at 14° in 20 μl reaction mixture, then transformed into *E. coli* strain 294. The plasmid DNA from six ampicillin resistant transformants was committed to restriction endonuclease analysis and one plasmid DNA, named pγCEAInt, demonstrated the correct construction of the C-terminal portion of gamma 1 (FIG. 5).

To obtain the N-terminal sequences, 30 μg of pγ298 was digested with Pst I and the 628 basepair DNA fragment encoding the N-terminal region of mouse anti-CEA gamma chain was isolated and purified. This fragment was further digested with Alu I and Rsa I for isolation of the 280 basepair fragment. A 15 nucleotide DNA primer

met glu val met leu
5' ATG GAA GTG ATG CTG 3'

was synthesized by the phosphotriester method (supra).

The 5' methionine serves as the initiation codon. 500 ng of this synthetic oligomer primer was phosphorylated at the 5' end in a reaction with 10 units T4 DNA kinase containing 0.5 mM ATP in 20 μl reaction mixture. ~500 ng of the 280 basepair Alu I-Rsa I DNA fragment was mixed with the phosphorylated primer. The mixture was heat denatured for 3 minutes at 95° and quenched in dry-ice ethanol. The denatured DNA solution was made 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4), 12 mM in each dNTP and 12 units DNA Polymerase I-Large Fragment was added. After 2 hours incubation at 37° C., this primer repair reaction was phenol/$CHCl_3$ extracted, ethanol precipitated, and digested to completion with HpaII. ~50 ng of the expected 125 basepair blund-end to Hpa II DNA fragment (fragment D) was purified from the gel.

A second aliquot of pγ298 DNA was digested with Pst I, the 628 basepair DNA fragment purified by polyacrylamide gel electrophoresis, and further digested with BamH I ahd Hpa II. The resulting 380 basepair fragment (fragment E) was purified by gel electrophoresis.

~5 μg of pγCEAIntI was digested with EcoR I, the cohesive ends were made flush with DNA polymerase I (Klenow), further digested with BamH I, treated with BAP and electrophoresed on a 6 percent polyacrylamide gel. The large vector fragment (fragment F) was isolated and purified.

In a three fragment ligation, 50 ng fragment D, 100 ng fragment E, and 100 ng fragment F were ligated overnight at 4° in a 20 μreaction mixture and used to transform *E. coli* K12 strain 294. The plasmid DNAs from 12 ampicillin resistant transformants were analyzed for the correct construction and the nucleotide sequence surrounding the initiation codon was verified to be correct for the plasmid named pγCEAInt2.

The expression plasmid, pγCEAtrp207-1* used for expression of the heavy chain gene is prepared by a 3-way ligation using the large vector fragment from pBR322(XAP) (supra) and two fragments prepared from pγCEAInt2.

pBR322(XAP) was treated as above by digestion with EcoR1, blunt ending with DNA polymerase (Klenow) in the presence of dNTPs, followed by digestion with Pst I, and isolation of the large vector fragment by gel electrophoresis. A 1543 base pair fragment from pγCEAInt2 containing trp promoter linked with the N-terminal coding region of the heavy chain gene was isolated by treating pγCEAInt2 with Pst I followed by BamH I, and isolation of the desired fragment using PAGE. The 869 base pair fragment containing the C-terminal coding portion of the gene was prepared by partial digestion of pγCEAInt2 with Ava I, blund ending with Klenow, and subsequent digestion with BamH I, followed by purification of the desired fragment by gel electrophoresis.

The aforementioned three fragments were then ligated under standard conditions using T4 DNA ligase, and a ligation mixture used to transform *E. coli* strain 294. Plasmid DNAs from several tetracycline resistant transformants were analyzed; one plasmid DNA demonstrated the proper construction and was designated pγCEAtrp207-1*.

E.1.9. Production of Immunoglobulin Chains by *E. coli*

*E. coli* strain W3110 (ATTC No. 27325) was transformed with pγCEAtrp207-1* or pKCEAtrp207-1* using standard techniques.

To obtain double transformants, *E. coli* strain W3110 cells were transformed with a modified pKCEAtrp207-1*, pKCEAtrp207-1*Δ, which had been modified by cleaving a Pst I-Pvu I fragment from the $amp^R$ gene and religating. Cells transformed with pKCEAtrp207-1*Δ are thus sensitive to ampicillin but still resistant to tetracycline. Successful transformants were retransformed using pγCEAInt2 which confers resistance to ampicillin but not tetracycline. Cells containing both pKCEAtrp207-1*Δ and pγCEAInt2 thus identified by growth in a medium containing both ampicillin and tetracycline.

To confirm the production of heavy and/or light chains in the transformed cells, the cell samples were inoculated into M9 tryptophan free medium containing 10 μg/ml tetracycline, and induced with indoleacrylic acid (IAA) when the OD 550 reads 0.5. The induced cells were grown at 37° C. during various time periods and then spun down, and suspended in TE buffer containing 2 percent SDS and 0.1M β-mercaptoethanol and boiled for 5 minutes. A 10× volume of acetone was added and the cells kept at 22° C. for 10 minutes, then centrifuged at 12,000 rpm. The precipitate was suspended in O'Farrell SDS sample buffer (O'Farrell, P. H., *J. Biol. Chem.*, 250: 4007 (1975)); boiled 3 minutes, recentrifuged, and fractionated using SDS PAGE (10 percent), and stained with silver stain (Goldman, D. et al., *Science* 211: 1437 (1981)); or subjected to Western blot using rabbit anti-mouse IgG (Burnett, W. N., et al., *Anal. Biochem.* 112: 195 (1981)), for identification light chain and heavy chain.

Cells transformed with pγCEAtrp207-1* showed bands upon SDS PAGE corresponding to heavy chain molecular weight as developed by silver stain. Cells transformed with pKCEAtrp207-1* showed the proper molecular weight band for light chain as identified by Western blot; double transformed cells showed bands for both heavy and light chain molecular weight proteins when developed using rabbit anti-mouse IgG by Western blot. These results are shown in FIGS. 8A, 8B, and 8C.

FIG. 8A shows results developed by silver stain from cells transformed with pγCEAtrp207-1*. Lane 1 is

monoclonal anti-CEA heavy chain (standard) from CEA.66-E3. Lanes 2b–5b are timed samples 2 hrs, 4 hrs, 6 hrs, and 24 hrs after IAA addition. Lanes 2a–5a are corresponding untransformed controls; Lanes 2c–5c are corresponding uninduced transformants.

FIG. **8B** shows results developed by Western blot from cells transformed with pKCEAtrp207-1*. Lanes 1b–6b are extracts from induced cells immediately, 1 hr, 3.5 hrs, 5 hrs, 8 hrs, and 24 hrs after IAA addition, and 1a–6a corresponding uninduced controls. Lane 7 is an extract from a pγCEAtrp207-1* control, lanes 8, 9, and 10 are varying amounts of anti CEA-kappa chain from CEA.66-E3 cells.

FIG. **8C** shows results developed by Western blot from four colonies of double tranformed cells 24 hours after IAA addition (lanes 4–7). Lanes 1–3 are varying amounts of monoclonal gamma chain controls, lanes 8 and 9 are untransformed and pγCEAtrp207-1* transformed cell extracts, respectively.

In another quantitative assay, frozen, transformed *E. coli* cells grown according to E.1.10 (below) were lysed by heating in sodium dodecyl sulfate (SDS)/β-mercaptoethanol cell lysis buffer at 100°. Aliquots were loaded on an SDS polyacrylamide gel next to lanes loaded with various amounts of hybridoma anti-CEA. The gel was developed by the Western blot, Burnett (supra), using $^{125}$I-labeled sheep anti-mouse IgG antibody from New England Nuclear. The results are shown in FIG. **9**. The figure shows that the *E. coli* products co-migrate with the authentic hybridoma chains, indicating no detectable proteolytic degradation in *E. coli*. Heavy chain from mammalian cells is expected to be slightly heavier than *E. coli* material due to glycosylation in the former. Using the hybridoma lanes as a standard, the following estimates of heavy and light chain production were made:

| | (Per gram of cells) |
|---|---|
| *E. coli* (W3110/pγCEAtrp207-1*) | 5 mg γ |
| *E. coli* (W3110/pKCEAtrp207-1*) | 1.5 mg K |
| *E. coli* (W3110/pKCEAtrp207-1*Δ, pγCEA Int2) | 0.5 mg K, 1.0 mg γ |

E.1.10 Reconstitution of Antibody from Recombinant K and Gamma Chains

In order to obtain heavy and light chain preparation for reconstitution, transformed cells were grown in larger batches, harvested and frozen. Conditions of growth of the variously transformed cells were as follows:

*E. coli* (W3110/pγCEAtrp207-1*) were inoculated into 500 ml LB medium containing 5 μg/ml tetracycline and grown on a rotary shaker for 8 hours. The culture was then transformed to 10 liters of fermentation medium containing yeast nutrients, salts, glucose, and 2 μg/ml tetracycline. Additional glucose was added during growth and at OD 550=20, indoleacrylic (IAA), a trp derepressor, was added to a concentration of 50 μg/ml. The cells were fed additional glucose to a final OD 550=40, achieved approximately 6 hours from the IAA addition.

*E. coli* (W3110) cells transformed with pKCEA trp 207-1* and double transformed (with pKCEAtrp207-1*Δ and pγCEAInt2) were grown in a manner analogous to that described above except that the OD 550 six hours after IAA addition at harvest was 25–30.

The cells were then harvested by centrifugation, and frozen.

E.2 Assay Method for Reconstituted Antibody

Anti-CEA activity was determined by ELISA as a criterion for successful reconstruction. Wells of microtiter plates (Dynatech Immulon) were saturated with CEA by incubation 100 μl of 2–5 μg CEA/ml solution in 0.1M carbonate buffer, pH 9.3 for 12 hours at room temperature. The wells were then washed 4 times with phosphate buffered saline (PBS), and then saturated with BSA by incubating 200 μl of 0.5 percent BSA in PBS for 2 hours at 37° C., followed by washing 4 times with PBS. Fifty microliters of each sample was applied to each well. A standard curve (shown in FIG. **10**), was run, which consisted of 50 μl samples of 10 μg, 5 μg, 1 μg, 500 ng, 100 ng, 50 ng, 10 ng, 5 ng and 1 ng anti-CEA/ml in 0.5 percent BSA in PBS, plus 50 μl of 0.5 percent BSA in PBS alone as a blank. All of the samples were incubated in the plate for 90 minutes at 37° C.

The plates were then washed 4 times with PBS, and sheep anti-mouse IgG-alkaline phosphate (TAGO, Inc.) was applied to each well by adding 100 μl of enzyme concentration of 24 units/ml in 0.5 percent BSA in PBS. The solution was incubated at 37° C. for 90 minutes. The plates wer washed 4 times with PBS before adding the substrate, 100 μl of a 0.4 mg/ml solution of p-nitrophenylphosphate (Sigma) in ethanolamine buffered saline, pH 9.5. The substrate was incubated 90 minutes at 37° C. for color development.

The $A_{450}$ of each well was read by the Microelisa Auto Reader (Dynatech) set to a threshold of 1.5, calibration of 1.0 and the 0.5 percent BSA in PBS (Blank) well set to 0.000. The $A_{450}$ data was tabulated in RS-1 on the VAX system, and the standard curve data fitted to a four-parameter logistic model. The unknown samples' concentrations were calculated based on the $A_{450}$ data.

E.3 Reconstruction of Recombinant Antibody and Assay

Frozen cells prepared as described in paragraph E.1.10 were thawed in cold lysis buffer [10 mM Tris HCl, pH 7.5, 1 mM EDTA, 0.1M NaCl, 1 mM phenylmethylsulfonyl fluoride (PMSF)] and lysed by sonication. The lysate was partially clarified by centrifugation for 20 mins at 3,000 rpm. The supernatant was protected from proteolytic enzymes by an additional 1 mM PmSF, and used immediately or stored frozen at −80° C.; frozen lysates were never thawed more than once.

The S-sulfonate of *E. coli* produced anti-CEA heavy chain (γ) was prepared as follows: Recombinant *E. coli* cells transformed with pγCEAtrp207-1* which contained heavy chain as insoluble bodies, were lysed and centrifuged as above; the pellet was resuspended in the same buffer, sonicated and re-centrifuged. This pellet was washed once with buffer, then suspended in 6M guanidine HCl, 0.1M Tris HCl, pH 8, 1 mM EDTA, 20 mg/ml sodium sulfite and 10 mg/ml sodium tetrathionate and allowed to react at 25° for about 16 hrs. The reaction mixture was dialyzed against 8M urea, 0.1M Tris HCl, pH 8, and stored at 4°, to give a 3 mg/ml solution of γ-$SSO_3$.

650 μl of cell lysate from cells of various *E. coli* strains producing various IgG chains, was added to 500 mg urea. To this was added β-mercaptoethanol to 20 mM, Tris-HCl, pH 8.5 to 50 mM and EDTA to 1 mM, and in some experiments, γ-$SSO_3$ was added to 0.1 mg/ml. After standing at 25° for 30–90 mins., the reaction mixtures were dialyzed at 4° against a buffer com-

posed of 0.1M sodium glycinate, pH 10.8, 0.5M urea, 10 mM glycine ethyl ester, 5 mM reduced glutathione, 0.1 mM oxidized glutathione. This buffer was prepared from $N_2$-saturated water and the dialysis was performed in a capped Wheaton bottle. After 16–48 hours, dialysis bags were transferred to 4° phosphate buffered saline containing 1 mM PMSF and dialysis continued another 16–24 hrs. Dialysates were assayed by ELISA as described in paragraph E.2 for ability to bind CEA. The results below show the values obtained by comparison with the standard curve in x ng/ml anti-CEA. Also shown are the reconstruction efficiencies calculated from the ELISA responses, minus the background (108 ng/ml) of cells producing K chain only, and from estimates of the levels of γ and K chains in the reaction mixtures.

| | ng/ml anti-CEA | Percent recombination |
|---|---|---|
| *E. coli* W3110 producing IFN-αA (control) | 0 | — |
| *E. coli* (W3110/pKCEAtrp207-1*) | 108 | — |
| *E. coli* (W3110/pKCEAtrp207-1*), plus γ-$SSO_3$ | 848 | 0.33 |
| *E. coli* (W3110/pKCEAtrp207-1*Δ, pγCEA Int2) | 1580 | 0.76 |
| Hybridoma anti-CEA K-$SSO_3$ and γ-$SSO_3$ | 540 | 0.40 |

E.4 Preparation of Chimeric Antibody

FIGS. 11 and 12 show the construction of an expression vector for a chimeric heavy (gamma) chain which comprises the murine anti CEA variable region and human γ-2 constant region.

A DNA sequence encoding the human gamma-2 heavy chain is prepared as follows: the cDNA libary obtained by standard techniques from a human multiple myeloma cell line is probed with 5' GGGCACT-CGACACAA 3' to obtain the plasmid containing the cDNA insert for human gamma-2 chain (Takahashi, et al., *Cell*, 29: 671 (1982), incorporated herein by reference), and analyzed to verify its identity with the known sequence in human gamma-2 (Ellison, J., et al., *Proc. Natl. Acad. Sci. (USA)*, 79: 1984 (1982) incorporated herein by reference).

As shown in FIG. 11, two fragments are obtained from this cloned human gamma 2 plasmid (pγ2). The first fragment is formed by digestion with PvuII followed by digestion with Ava III, and purification of the smaller DNA fragment, which contains a portion of the constant region, using 6 percent PAGE. The second fragment is obtained by digesting the pγ2 with any restriction enzyme which cleaves in the 3' untranslated region of γ2, as deduced fromthe nucleotide sequence, filling in with Klenow and dNTPs, cleaving with Ava III, and isolating the smaller fragment using 6 percent PAGE. (The choice of a two step, two fragment composition to supply the PvuII-3' untranslated fragment provides a cleaner path to product due to the proximity of the AVAIII site to the 3 terminal end thus avoiding additional restriction sites in the gene sequence matching the 3' untranslated region site.) pγCEA207-1* is digested with EcoR 1, treated with Klenow and dNTPs to fill in the cohesive end, and digested with Pvu II, the large vector fragment containing promoter isolated by 6 percent PAGE.

The location and DNA sequence surrounding the PvuII site in the mouse gamma-1 gene are identical to the location and DNA sequence surrounding the PvuII site in the human gamma-2 gene.

The plasmid resulting from a three way ligation of the foregoing fragments, pChim1, contains, under the influence of trp promoter, the variable and part of the constant region of murine anti-CEA gamma 1 chain, and a portion of the gamma 2 human chain. pChim1 will, in fact, express a chimeric heavy chain when tranformed into *E. coli*, but one wherein the change from mouse to human does not take place at the variable to constant junction.

FIG. 12 shows modification of pChim1 to construct pChim2 so that the resulting protein from expression will contain variable region from murine anti CEA antibody and constant region from the human γ-2 chain. First, a fragment is prepared from pChim1 by treating with Nco I, blunt ending with Klenow and dNTPs, cleaving with Pvu II, and isolating the large vector fragment which is almost the complete plasmid except for short segment in the constant coding region for mouse anti CEA. A second fragment is prepared from the previously described pγ2 by treating with Pvu II, followed by treating with any restriction enzyme which cleaves in the variable region, blunt ending with Klenow and dNTPs and isolating the short fragment which comprises the junction between variable and constant regions of this chain.

Ligation of the foregoing two fragments produces an intermediate plasmid which is correct except for an extraneous DNA fragment which contains a small portion of the constant region of the murine anti CEA antigen, and a small portion of the variable region of the human gamma chain. This repair can be made by excising the Xba I to Pvu II fragment and cloning into M13 phage as described by Messing et al., *Nucleic Acids Res.* 9: 309 (1981), followed by in vitro site directed deletion mutagenesis as described by Adelman, et al., DNA, in press (1983) which is incorporated herein by reference. The Xba I-Pvu II fragment thus modified is ligated back into the intermediate plasmid to form pChim2. this plasmid then is capable of expressing in a suitable host a cleanly constructed murine variable/human constant chimeric heavy chain.

In an analogous fashion, but using mRNA templates for cDNA construction for human kappa rather than γ chain, the expression plasmid for chimeric light chain is prepared.

The foregoing two plasmids are then double transformed into *E. coli* W3110, the cells grown and the chains reconstituted as set forth in paragraph E.1–E.3 supra.

E.5 Preparation of Altered Murine Anti-CEA Antibody

E.5.1 Construction of Plasmid Vectors for Direct Expression of Altered Murine Anti-CEA Heavy Chain Gene

The cysteine residues, and the resultant disulfide bonds in the region of amino acids 216–230 in the constant region of murine anti-CEA heavy chain are suspected to be imported for complement fixation (Klein, et al., *Proc. Natl. Acad. Sci., (USA)*, 78: 524 (1981)) but not for the antigen binding property of the resulting antibody. To decrease the probability of incorrect disulfide bond formation during reconstruction according to the process of the invention herein, the nucleotides encoding the amino acid residues 226–232 which includes codons for three cysteines, are deleted as follows:

A "deleter" deoxyoligonucelotide, 5' CTAACAC-CATGTCAGGGT is used to delete the relevant portions of the gene from pγCEAtrp207-1* by the procedure of Wallace, et al., *Science*, 209: 1396 (1980). Briefly, the "deleter" deoxyoligonucelotide is annealed with denatured pγCEAtrp207-1* DNA, and primer repair synthesis carried out in vitro, followed by screening by hybridization of presumptive deletion clones with $P^{32}$ labelled deleter sequence.

E.5.2 Production of Cysteine Deficient Altered Antibody

The plasmid prepared in E.5.1 is transformed into an *E.coli* strain previously transformed with pKCEAtrp207-1* as described above. The cells are grown, extracted for recombinant antibody chains, and the altered antibody reconstituted as described in E.1.10.

E.6 Preparation of Fab

E.6.1 Construction of a Plasmid Vector for Direct Expression of Murine Anti-CEA Gamma 1 Fab Fragment Gene pγCEAFabtrp207-1*

FIG. 13 presents the construction of pγCEA-Fabtrp207-1*. 5 μg of pBR322 was digested with Hind III, the cohesive ends made flush by treating with Klenow and dNTPs; digested with Pst I, and treated with BAP. The large vector fragment, fragment I, was recovered using 6 percent PAGE followed by electroelution.

5 μg of pγCEAtrp207-1* was digested with both BamH I and Pst I and the ~1570 bp DNA fragment (fragment II) containing the trp promoter and the gene sequence encoding the variable region continuing into constant region and further into the anti-CEA gamma 1 chain hinge region, was isolated and purified after electrophoresis.

Expression of the anti-CEA gamma 1 chain Fab fragment rather than complete heavy chain requires that a termination condon be constructed at the appropriate location in the gene. For this, the 260 bp Nco I-Nde I DNA fragment from 20 μg of the pγ298 was isolated and purified. A 13 nucleotide DNA primer, the complement of which encodes the last 3 C-terminal amino acids of the Fab gene and 2 bases of the 3 needed for the stop codon, was synthesized by the phosphotriester method (supra). The probe hybridizes to nucleotides 754 to 767 (FIG. 4) which has the following sequence:

Asp Cys Gly Stop
5' GGGATTGTGGTTG 3'

The third base of the stop codon is provided by the terminal nucleotide of the filled-in Hind III site from pBR322 cleavage described above. 500 ng of this primer was used in a primer repair reaction by phosphorylation at the 5' end in a reaction with 10 units T4 DNA kinase containing 0.5 mM ATP in 20 μl, and mixing with ~200 ng of the Nco I-Nde I DNA fragment. The mixture was heat denatured for 3 minutes at 95° and quenched in dry-ice ethanol. The denatured DNA solution was made 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4), 12 mM in each dNTP and 12 units DNA Polymerase I-Large Fragment was added. After 2 hours incubation at 37° C., this primer repair reaction was phenol/$CHCl_3$ extracted, ethanol precipitated, digested with BamH I and the reaction electrophoresed through a 6 percent polyacrylamide gel. ~50 ng of the 181 bp blunt end to BamH I DNA fragment, fragment III, was isolated and purified.

~100 ng of fragment I, ~100 ng each of fragments II and III were ligated overnight and transformed into *E. coli* K12 strain 294. Plasmid DNA from several tetracycline resistant transformants was analyzed for the proper construction and the nucleotide sequence through the repair blunt end filled-in Hind III junction was determined for verification of the TGA stop codon.

E.6.2 Production of Fab Protein

The plasmid prepared in E.6.1 is transformed into an *E. coli* strain previously transformed with pKCEAtrp207-1* as described above. The cells are grown, extracted for recombinant antibody chains and the Fab protein reconstituted as described in E.1.10.

We claim:

1. A method comprising
   (a) preparing a DNA sequence encoding a chimeric immunoglobulin heavy or light chain having specificity for a particular known antigen wherein a constant region is homologous to the corresponding constant region of an antibody of a first mammalian species and a variable region thereof is homologous to the variable region of an antibody derived from a second, different mammalian species;
   (b) inserting the sequence into a replicable expression vector operably linked to a suitable promoter compatible with a host cell;
   (c) transforming the host cell with the vector of (b);
   (d) culturing the host cell; and
   (e) recovering the chimeric heavy or light chain from the host cell culture.

2. The method of claim 1 wherein the first mammalian species is human.

3. A composition comprising a chimeric immunoglobulin heavy or light chain having specificity for a particular known antigen having a constant region homologous to a corresponding constant region of an antibody of a first mammalian species and a variable region homologous to a variable region of an antibody derived from a second, different mammalian species.

4. The chimeric heavy or light chain of clain 3 wherein the constant region is human.

5. A replicable expression vector comprising DNA operably linked to a promoter compatible with a suitable host cell, said DNA encoding a chimeric immunoglobulin heavy or light chain having specificity for a particular known antigen and having a constant region homologous to a corresponding region of an antibody of a first mammalian species and a variable region homologous to a variable region of an antibody derived from a second, different mammalian species.

6. The vector of claim 5 wherein the first mammalian species is human.

7. Recombinant host cells transformed with the vector of claim 5.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

# CERTIFICATE OF CORRECTION

PATENT NO. : 4,816,567 Page 1 of 3

DATED : March 28, 1989

INVENTOR(S) : Shmuel Cabilly et al.

It is certified that error appears in the above - identified patent and that said Letters Patent is hereby corrected as shown below:

On the title page, left col. line 10, insert in addition to "Assignee: Genentech, Inc.", --City of Hope, Duarte, Calif.--.

On Col. 5, line 10, change "immunoglobuins" to --immunoglobulins--.

On Col. 1, line 17, insert --,-- after "proteins".

On Col. 4, line 9, change "reach" to --reached--.

On Col. 5, line 14, delete ".".

On Col. 6, line 28, delete the second "antibodies".

On col. 6, line 32, change "reference" to --referenced--.

On Col. 7, line 8, change "respones" to --responses--.

On Col. 9, line 7, change "$F^{32}$" to --$F^{-}$--.

On Col. 10, line 21, change "Examlples" to --Examples--.

On Col. 16, line 1, change "particular" to --particularly--.

On Col. 16, line 54, change "formaion" to --formation--.

On Col. 17, line 38, change "liner" to --linear--.

On Col. 17, line 62, change "for" to --from--.

On Col. 18, line 38, change "mous" to --mouse--.

On Col. 19, line 27, change "from" to --for--.

On Col. 20, line 57, change "207-1," to --207-1.--.

On Col. 21, line 6, change "(pH 7.4)" to --(pH 7.4),--.

On Col. 21, line 21, change "isolted" to --isolated--.

On Col. 21, line 23, change "precipitaion" to --precipitation--.

On Col. 21, line 23, change "resuspensionin" to --resuspension in--.

On Col. 21, line 58, change "sequene" to --sequence--.

On Col. 22, line 5, change "isoated" to --isolated--.

UNITED STATES PATENT AND TRADEMARK OFFICE

# CERTIFICATE OF CORRECTION



PATENT NO. : 4,816,567

DATED : March 28, 1989

INVENTOR(S) : Shmuel Cabilly et al.

It is certified that error appears in the above - identified patent and that said Letters Patent is hereby corrected as shown below:

On Col. 22, line 19, change "reactin" to --reaction--.

On Col. 22, line 25, change "digested" to --designated--.

On Col. 22, line 30, change "PvaII" to --PvuII--.

On Col. 22, line 54, change "regin" to --region--.

On Col. 23, line 44, change "ahd" to --and--.

On Col. 23, line 55, change "μreaction" to --μl reaction--.

On Col. 24, line 9, change "blund" to --blunt--.

On Col. 25, line 16, change "tranformed" to --transformed--.

On Col. 25, line 47, change "preparation" to --preparations--.

On Col. 25, line 55, change "transformed" to --transferred--.

On Col. 26, line 5, change "reconstruction" to --reconstitution--.

On Col. 26, line 7, change "incubation" to --incubating--.

On Col. 26, line 25, change "wer" to --were--.

On Col. 27, line 12, change "reconstruction" to --reconstitution--.

On Col. 27, line 37, change "myleoma" to --myeloma--.

On Col. 27, line 60, change "AVAIII" to --AvaIII--.

On Col. 28, line 64, change "reconstruction" to --reconstitution--.

On Col. 29, line 38, change "condon" to --codon--.

On Col. 30, line 48, change "clain" to --claim--.

On Col. 30, line 55, insert --constant-- between "corresponding" and "region".

# UNITED STATES PATENT AND TRADEMARK OFFICE
# CERTIFICATE OF CORRECTION

PATENT NO. : 4,816,567 Page 3 of 3

DATED : March 28, 1989

INVENTOR(S) : Shmuel Cabilly, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On Col. 21, line 58, change "sequene" to --sequence--.

On Col. 22, line 5, change "isoated" to --isolated--.

**Signed and Sealed this**

**Fourth Day of August, 1992**

*Attest:*

DOUGLAS B. COMER

*Attesting Officer*

*Acting Commissioner of Patents and Trademarks*

US006331415B1

(12) **United States Patent**
**Cabilly et al.**

(10) **Patent No.: US 6,331,415 B1**
(45) **Date of Patent: Dec. 18, 2001**

(54) **METHODS OF PRODUCING IMMUNOGLOBULINS, VECTORS AND TRANSFORMED HOST CELLS FOR USE THEREIN**

(75) Inventors: **Shmuel Cabilly**, Monrovia; **Herbert L. Heyneker**, Burlingame; **William E. Holmes**, Pacifica; **Arthur D. Riggs**, La Verne; **Ronald B. Wetzel**, San Francisco, all of CA (US)

(73) Assignee: **Genentech, Inc.**, South San Francisco, CA (US)

( * ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **07/205,419**

(22) Filed: **Jun. 10, 1988**

**Related U.S. Application Data**

(63) Continuation of application No. 06/483,457, filed on Apr. 8, 1983, now Pat. No. 4,816,567.

(51) **Int. Cl.**[7] ..... **C12N 15/13**; C12N 15/00; C12N 15/63

(52) **U.S. Cl.** ..... **435/69.6**; 435/69.1; 435/69.7; 435/70.1; 435/70.21; 435/71.1; 435/71.2; 435/320; 435/252.1; 435/252.3; 435/252.33; 435/254.11; 435/254.2; 435/254.21; 435/455; 435/471; 435/483; 435/485

(58) **Field of Search** ..... 435/69.1, 69.7, 435/71.1, 70.1, 71.2, 320, 261, 252.1, 252.3, 81, 55, 56, 69.6, 252.33, 254.21, 483

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(57) **ABSTRACT**

The invention relates to processes for producing an immunoglobulin or an immunologically functional immunoglobulin fragment containing at least the variable domains of the immunoglobulin heavy and light chains. The processes can use one or more vectors which produce both the heavy and light chains or fragments thereof in a single cell. The invention also relates to the vectors used to produce the immunoglobulin or fragment, and to cells transformed with the vectors.

**36 Claims, 19 Drawing Sheets**

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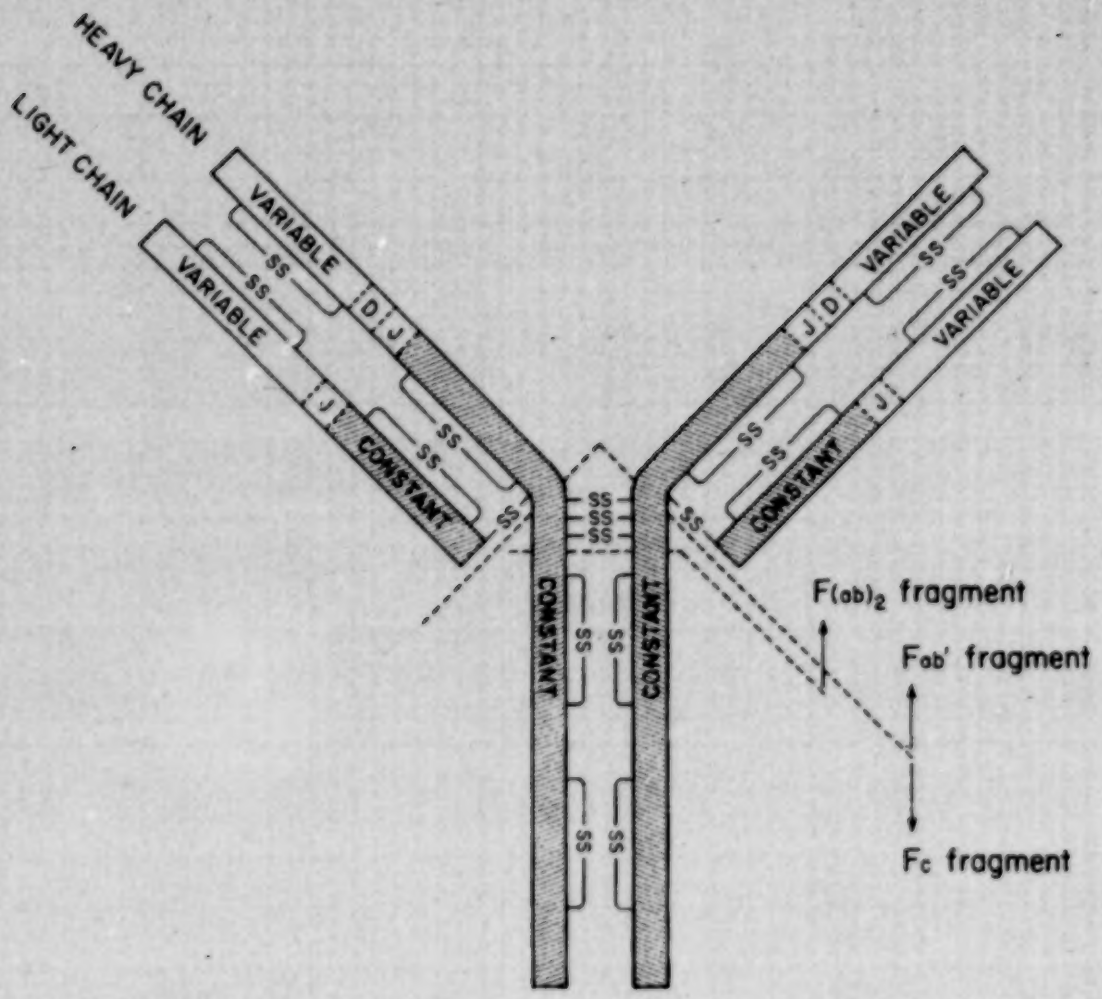


Fig. 1.

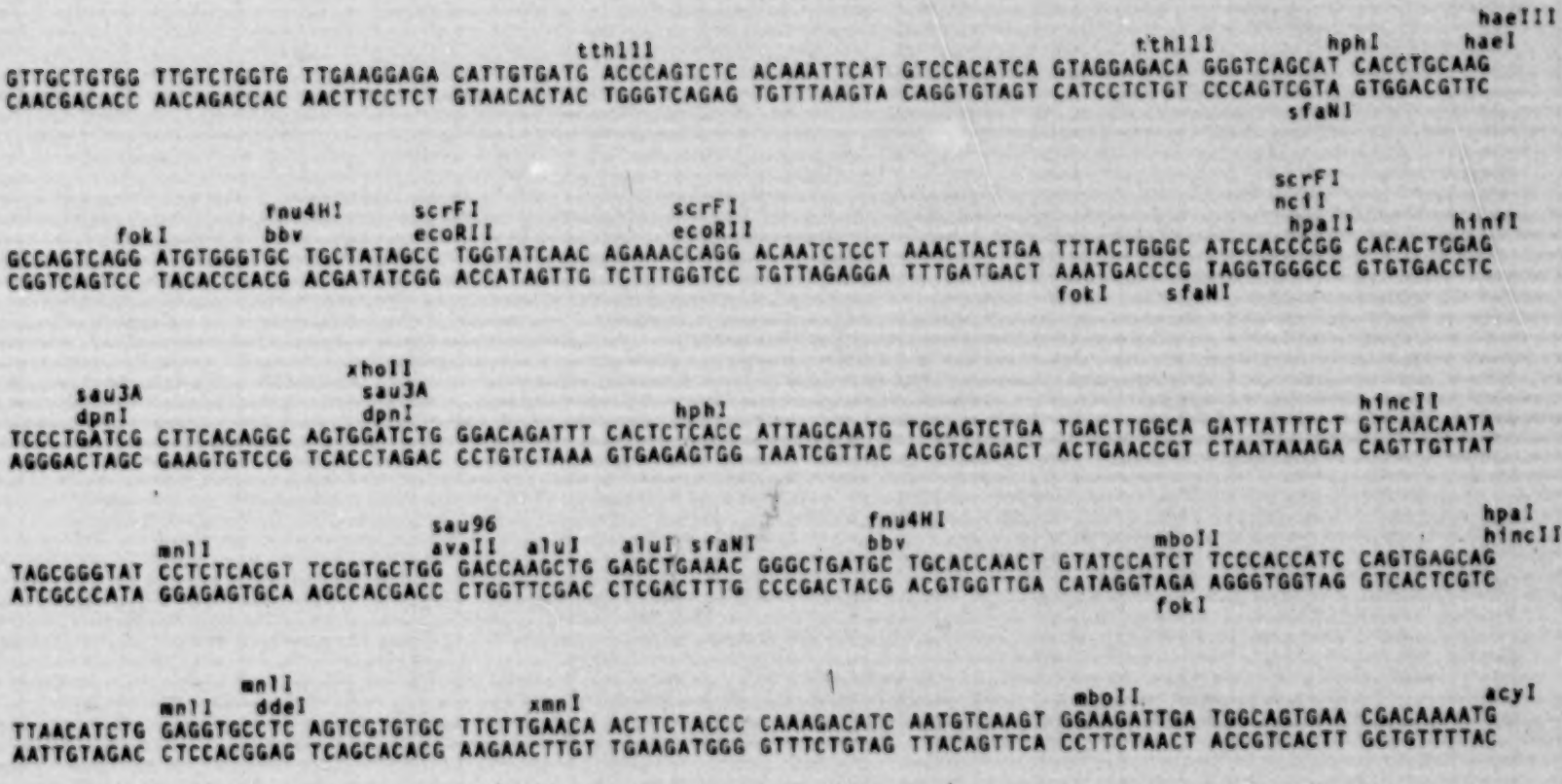
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Fig. 2A.

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                                dpnI                                    fnu4HI
        hgaI                  bclI                                      bbv     mnlI  hincII                                  aluI
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        CGCAGGACTT GTCAACCTGA CTAGTCCTGT CGTTTCTGTC GTGGATGTCG TACTCGTCGT GGGAGTGCAA CTGGTTCCTG CTCATACTTG CTGTATTGTC

                    mnlI                                                                                sau96   hgaI
                      haeIII                                                                              ddeI
                     haeI                          hphI            aluI                                 avaII   acyI
601     CTATACCTGT GAGGCCACTC ACAAGACATC AACTTCACCC ATTGTCAAGA GCTTCAACAG GAATGAGTGT TAGAGACAAA GGTCCTGAGA CGCCACCACC
        GATATGGACA CTCCGGTGAG TGTTCTGTAG TTGAAGTGGG TAACAGTTCT CGAAGTTGTC CTTACTCACA ATCTCTGTTT CCAGGACTCT GCGGTGGTGG

                                                                                                                mnlI
        aluI    aluI          mboII    ddeI         mnlI                                    hgiA        mnlI        mnlI
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        TCGAGGGGTC GAGGTAGGAT AGAAGGGAAG ATTCCAGAAC CTCCGAAGGG GTGTTCGCTG GATGGTGACA ACGCCACGAG GTTTGGAGGA GGGGTGGAGG
            fokI

              mnlI
            mnlI   mnlI                                        xmnI                 hinfI
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Fig. 2B.

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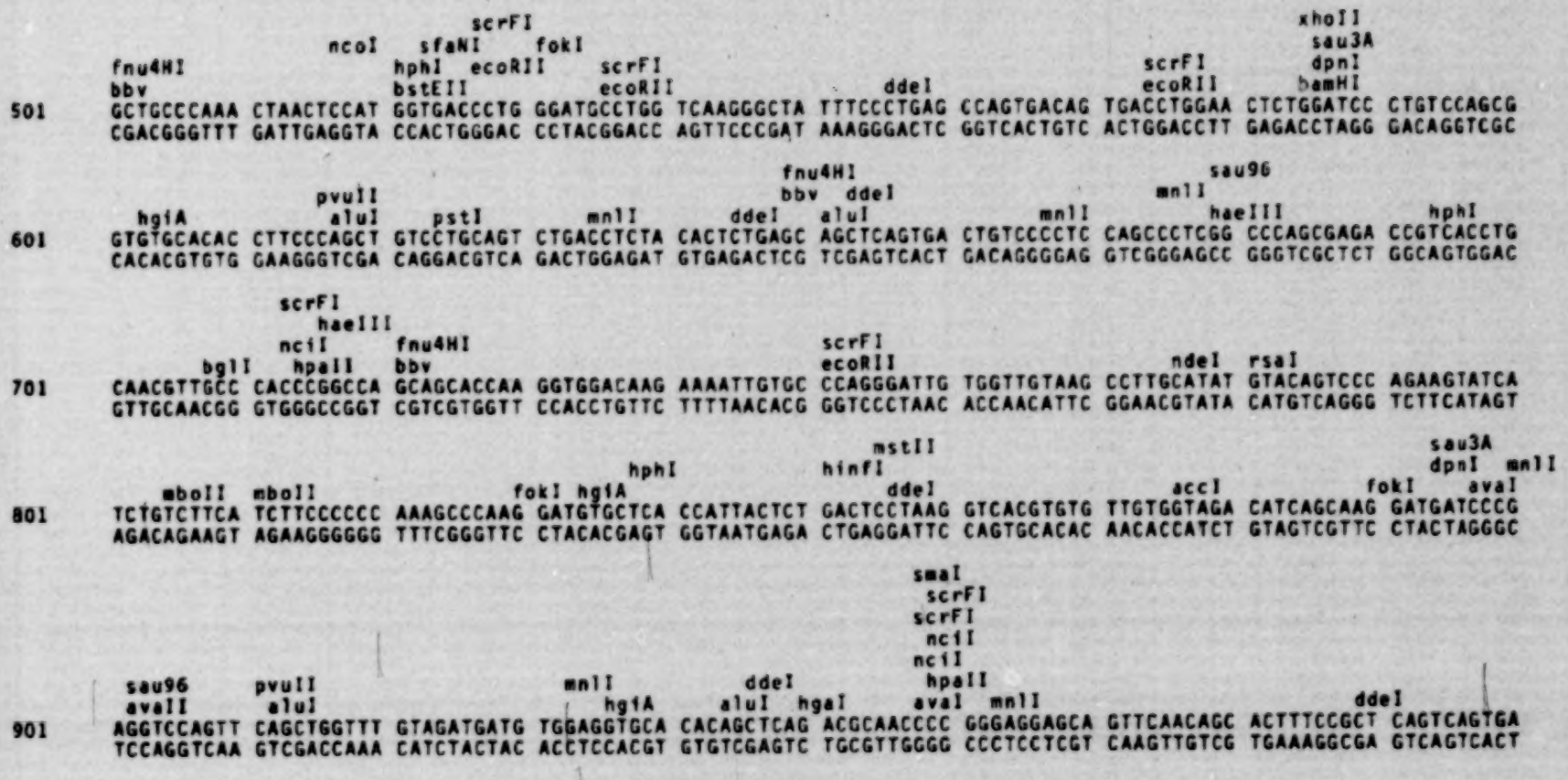
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Fig. 4B.

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                                280                                     290                                     300
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                                310                                     320                                     330
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                                340                                     350                                     360
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                                370                                     380                                     390
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                                400                                     410                                     420
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                                430                                     440                         447
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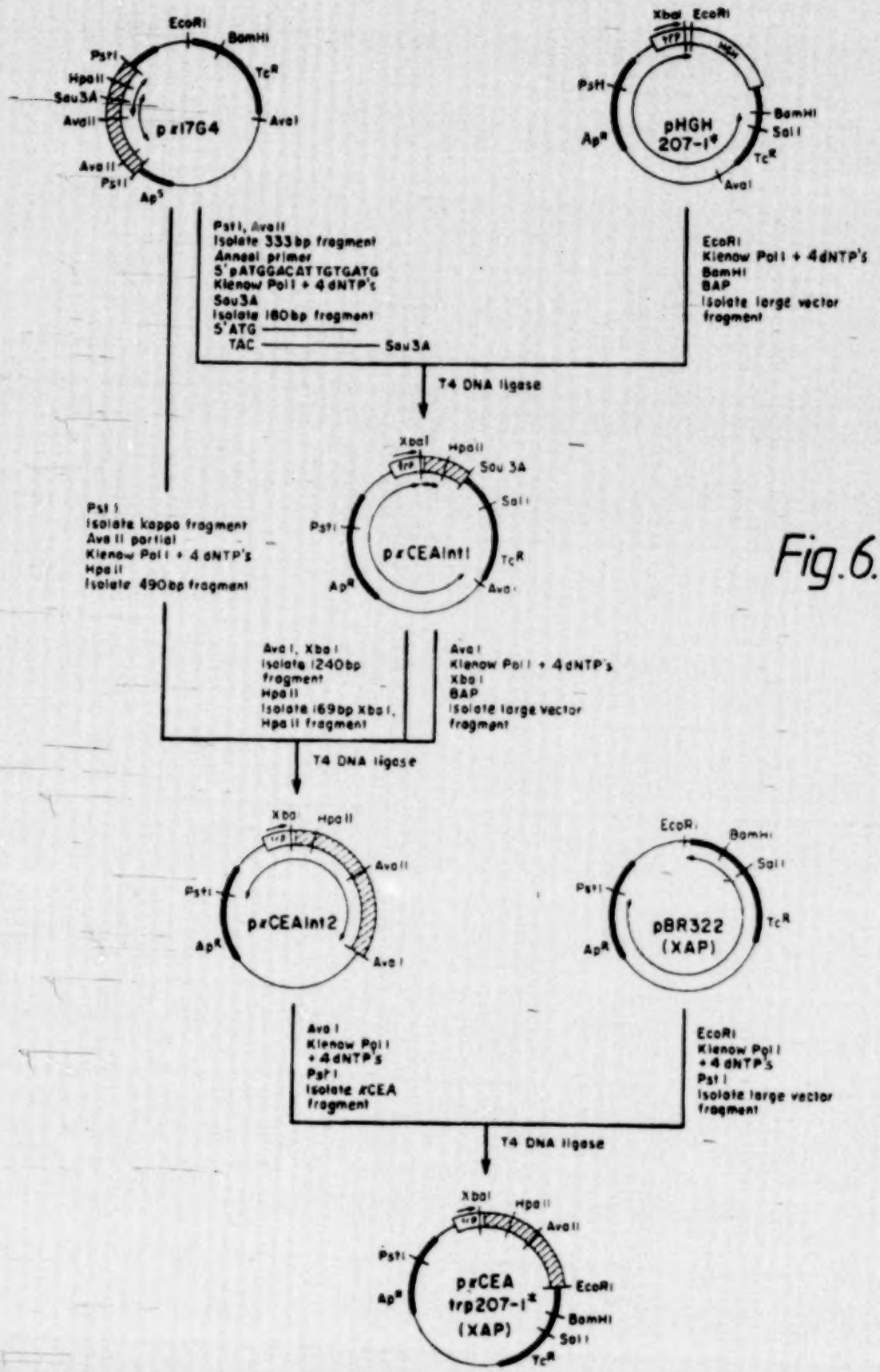
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Klenow PolI + 4 dNTP's
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SalI
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TcR
ApR
AvaI
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PstI
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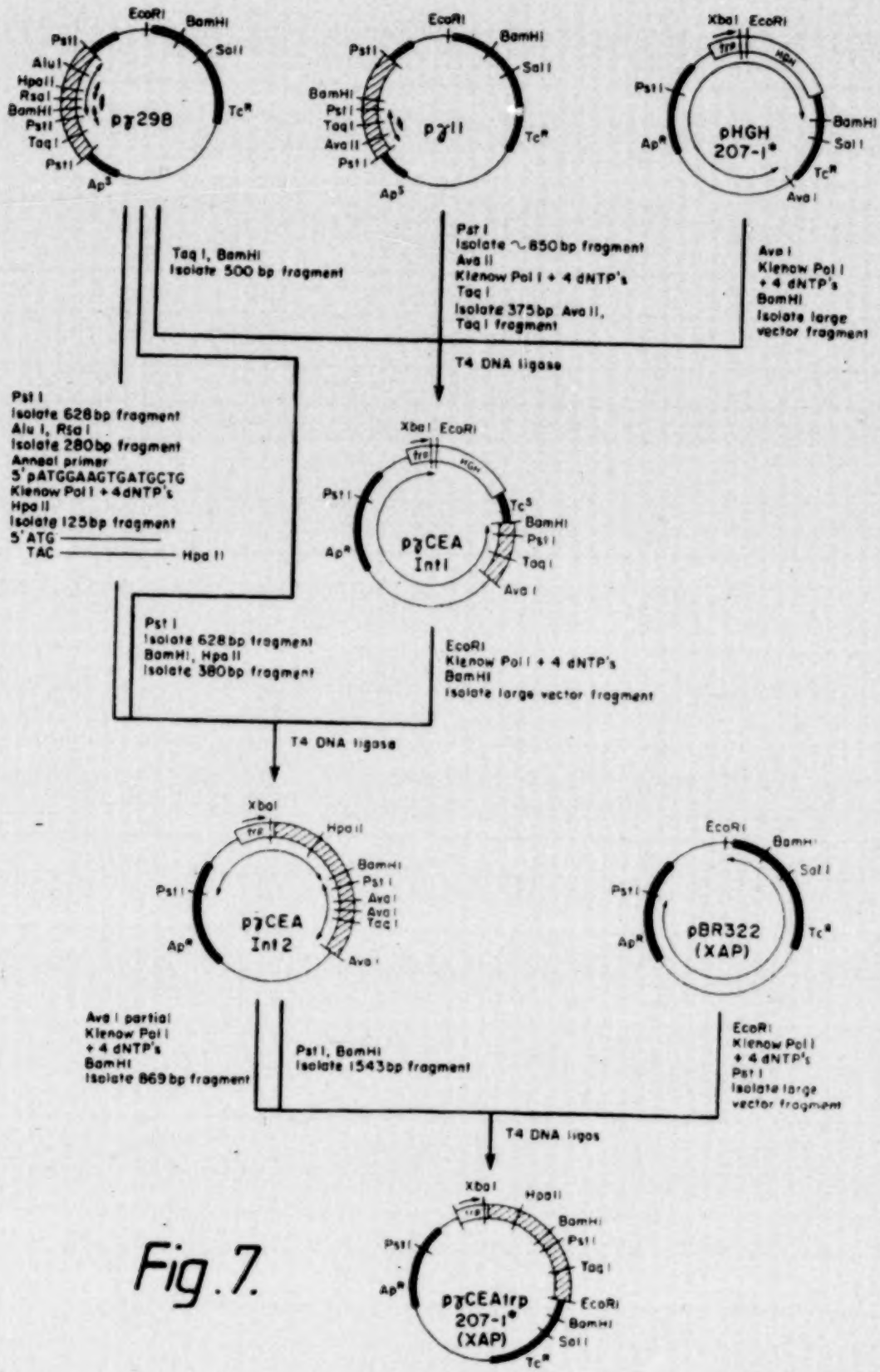
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Taq I
pBR322 (XAP)
Ava I partial
Klenow Pol I
+ 4 dNTP's
BamHI
Isolate 869 bp fragment
Pst I, BamHI
Isolate 1543 bp fragment
EcoRI
Klenow Pol I
+ 4 dNTP's
Pst I
Isolate large vector fragment
T4 DNA ligas
pγCEAIrp 207-1* (XAP)

Fig. 7.

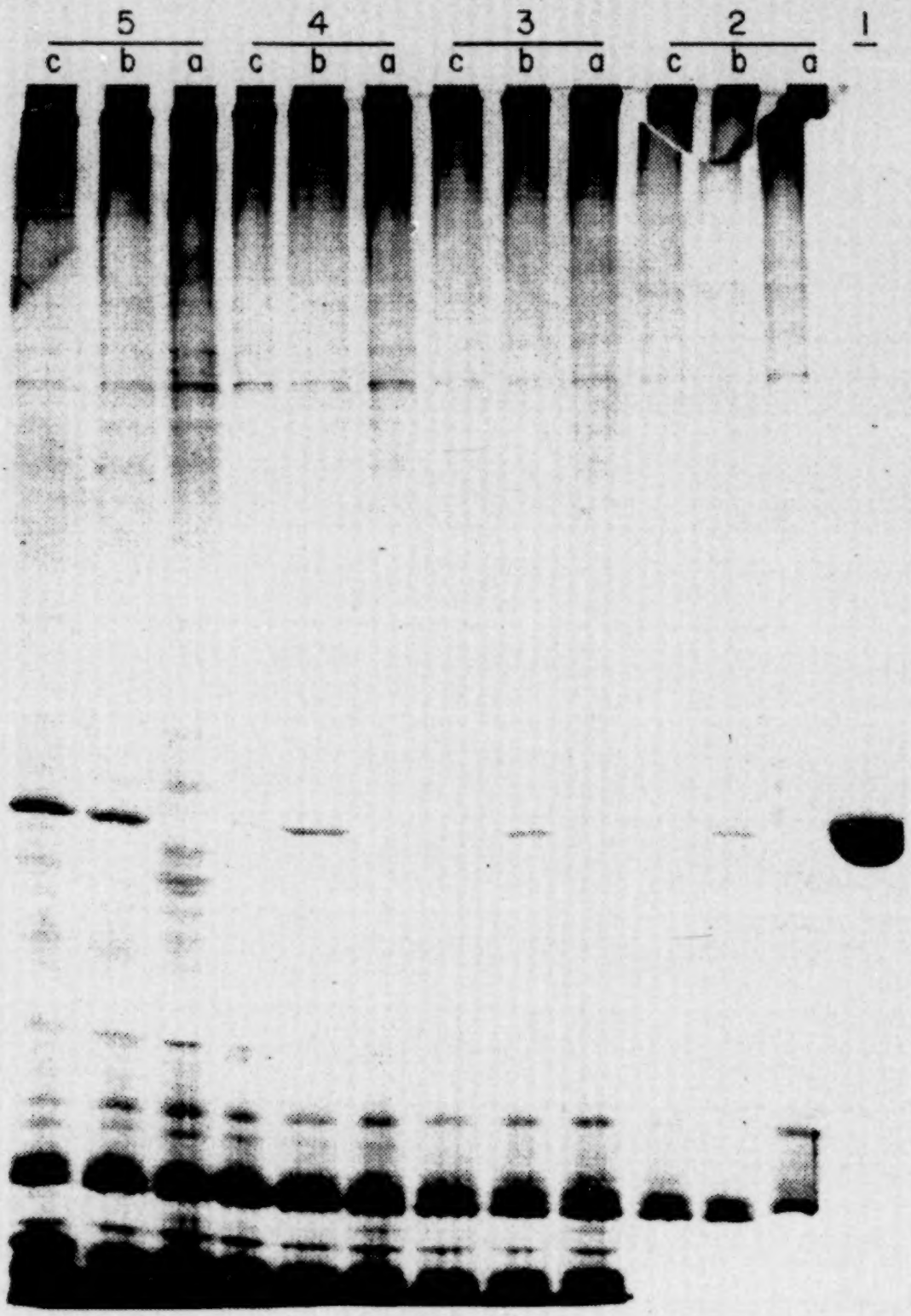


Fig. 8A.

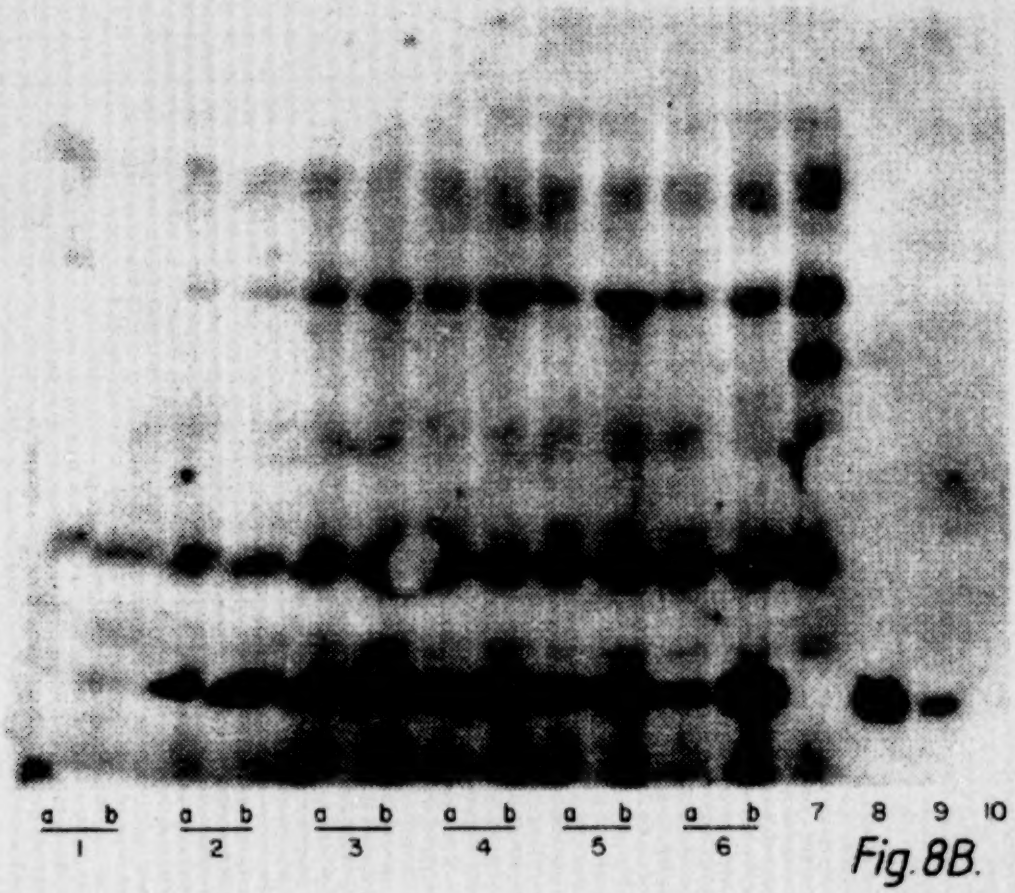


Fig. 8B.

Fig. 8C.

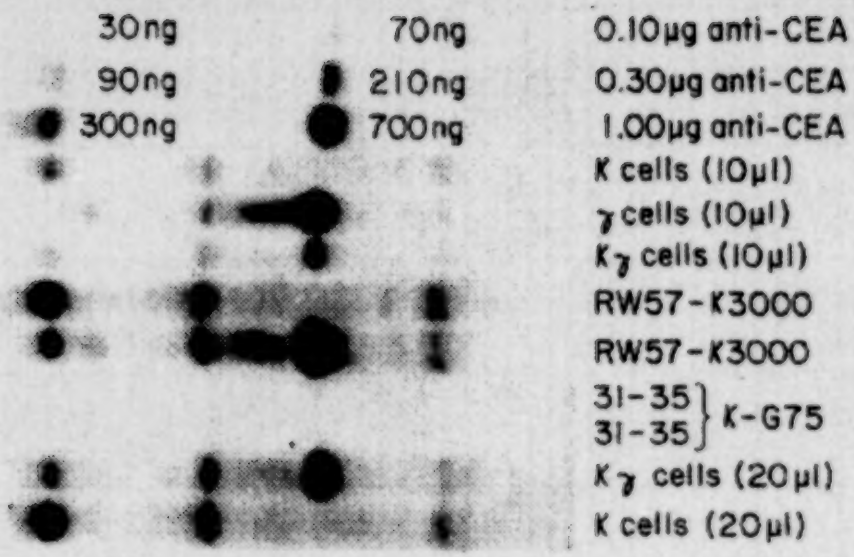
30ng
70ng
0.10μg anti-CEA
90ng
210ng
0.30μg anti-CEA
300ng
700ng
1.00μg anti-CEA
K cells (10μl)
γ cells (10μl)
Kγ cells (10μl)
RW57-K3000
RW57-K3000
31-35
31-35
K-G75
Kγ cells (20μl)
K cells (20μl)

Fig. 9.

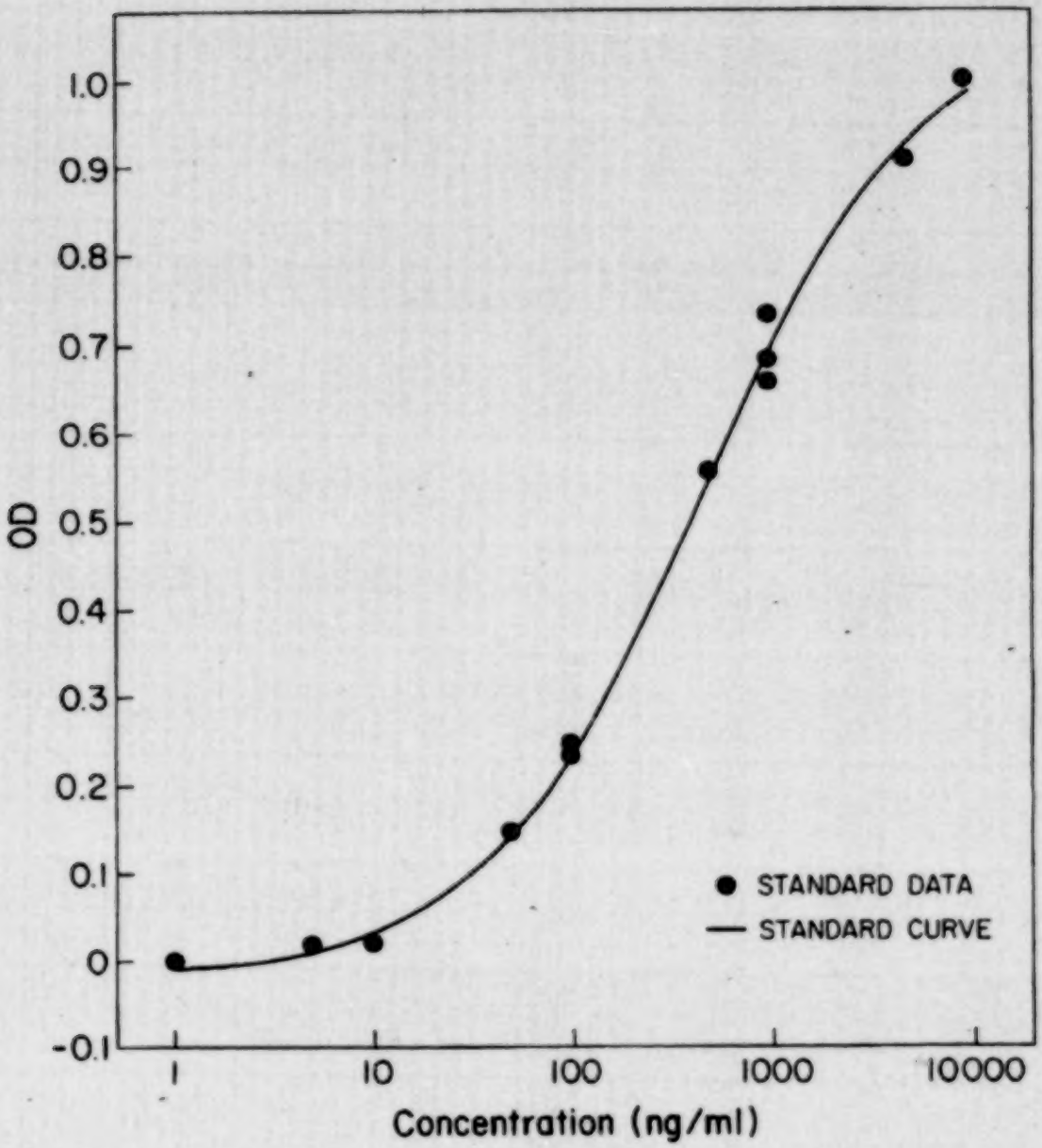
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
OD
1
10
100
1000
10000
Concentration (ng/ml)
STANDARD DATA
STANDARD CURVE

Fig. 10.

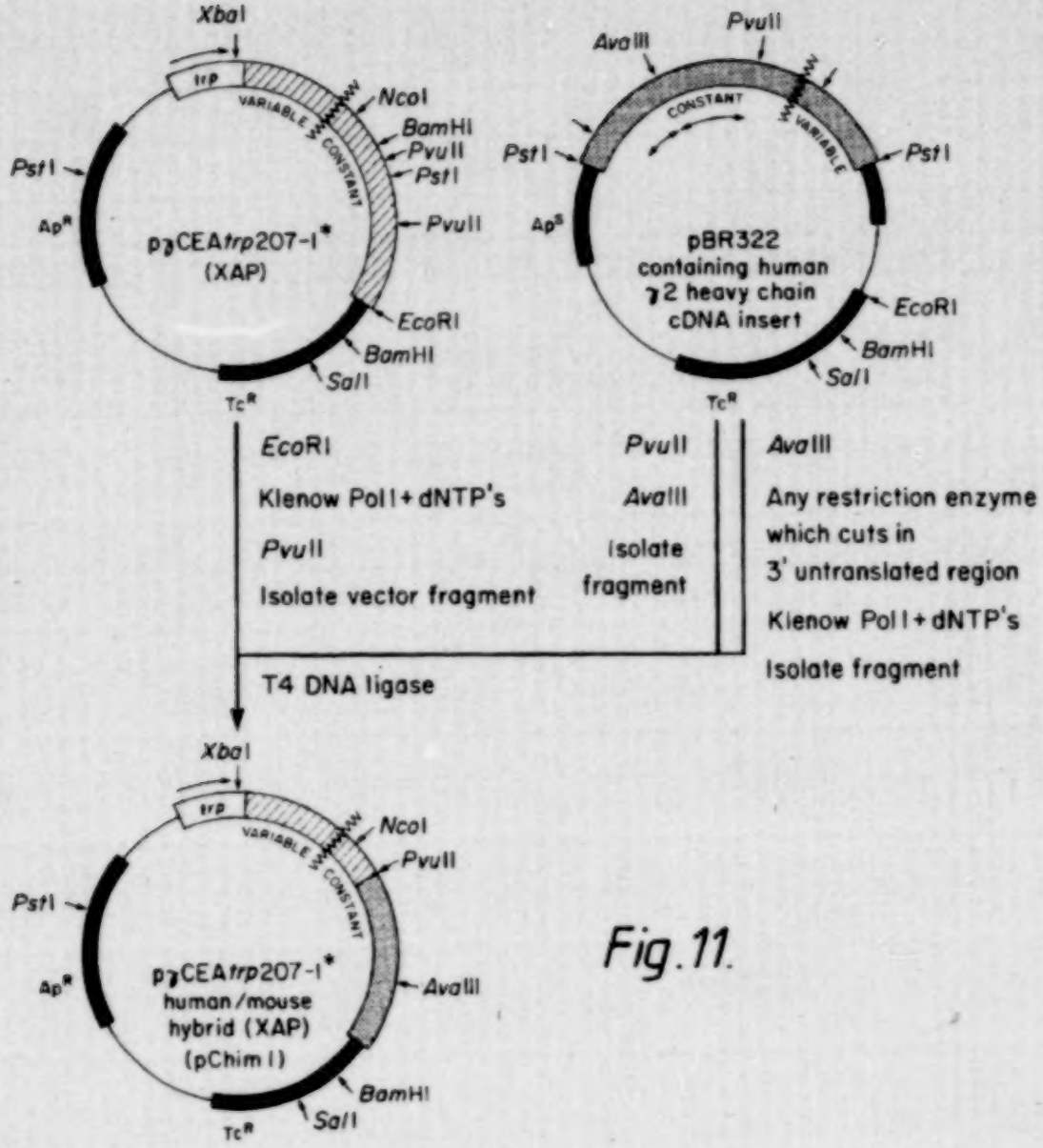
XbaI
trp
VARIABLE
CONSTANT
NcoI
BamHI
PvuII
PstI
PvuII
EcoRI
BamHI
SalI
PstI
Ap^R
pγCEAtrp207-1*
(XAP)
Tc^R
AvaIII
PvuII
CONSTANT
VARIABLE
PstI
PstI
Ap^S
pBR322
containing human
γ2 heavy chain
cDNA insert
EcoRI
BamHI
SalI
Tc^R
EcoRI
Klenow PolI + dNTP's
PvuII
Isolate vector fragment
PvuII
AvaIII
Isolate
fragment
AvaIII
Any restriction enzyme
which cuts in
3' untranslated region
Klenow PolI + dNTP's
Isolate fragment
T4 DNA ligase
XbaI
trp
VARIABLE
CONSTANT
NcoI
PvuII
PstI
AvaIII
Ap^R
pγCEAtrp207-1*
human/mouse
hybrid (XAP)
(pChim I)
BamHI
SalI
Tc^R

Fig. 11.

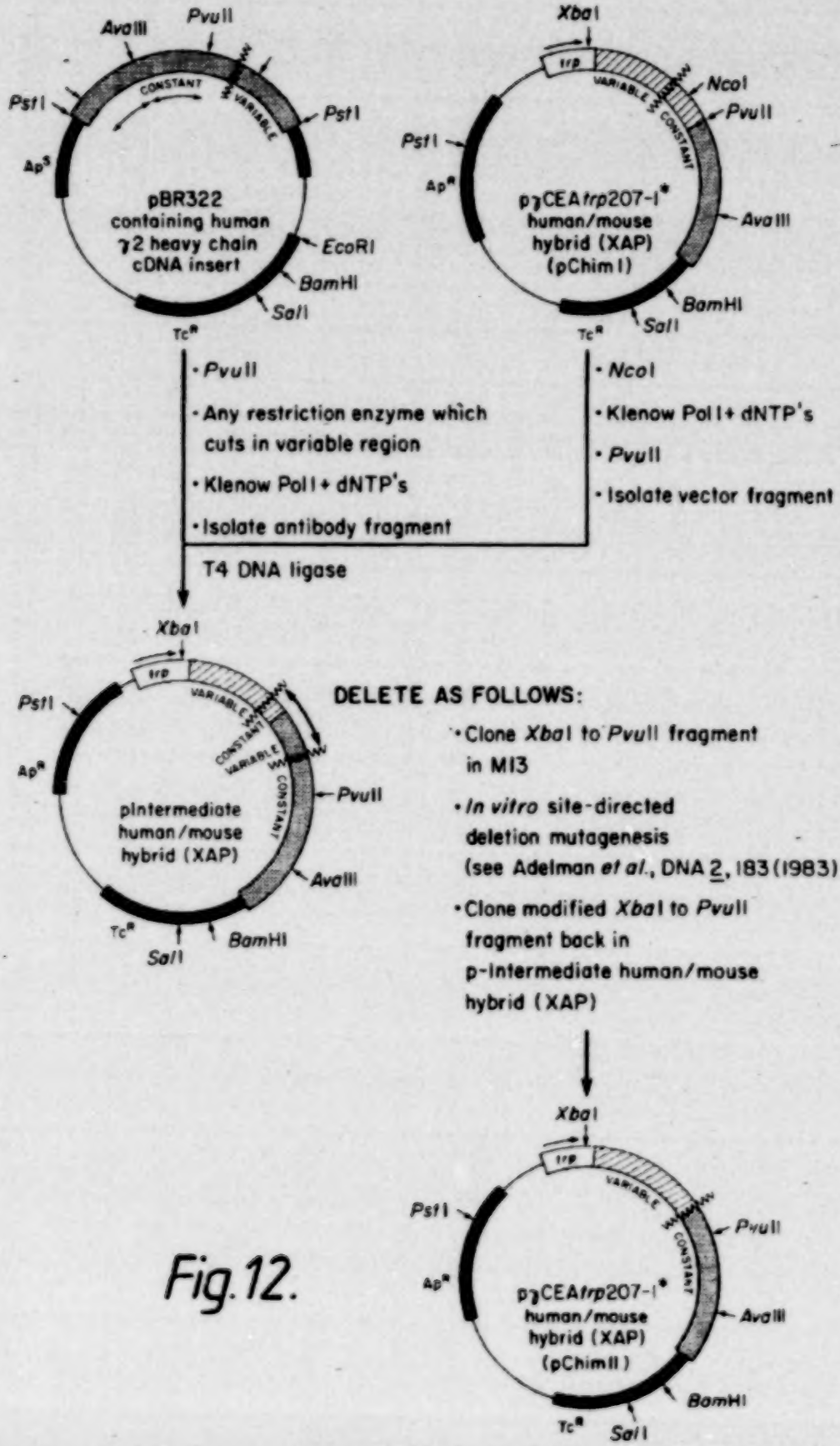
AvaIII
PvuII
PstI
PstI
Ap^R
CONSTANT
VARIABLE
pBR322
containing human
γ2 heavy chain
cDNA insert
EcoRI
BamHI
SalI
Tc^R
XbaI
trp
VARIABLE
CONSTANT
NcoI
PvuII
PstI
Ap^R
pγCEAtrp207-1*
human/mouse
hybrid (XAP)
(pChim1)
AvaIII
BamHI
SalI
Tc^R
• PvuII
• Any restriction enzyme which cuts in variable region
• Klenow Pol I + dNTP's
• Isolate antibody fragment
• NcoI
• Klenow Pol I + dNTP's
• PvuII
• Isolate vector fragment
T4 DNA ligase
XbaI
trp
VARIABLE
CONSTANT
VARIABLE
CONSTANT
PstI
Ap^R
PvuII
pIntermediate
human/mouse
hybrid (XAP)
AvaIII
Tc^R
SalI
BamHI
DELETE AS FOLLOWS:
• Clone XbaI to PvuII fragment in M13
• In vitro site-directed deletion mutagenesis (see Adelman et al., DNA 2, 183 (1983))
• Clone modified XbaI to PvuII fragment back in p-Intermediate human/mouse hybrid (XAP)
XbaI
trp
VARIABLE
CONSTANT
PstI
PvuII
Ap^R
pγCEAtrp207-1*
human/mouse
hybrid (XAP)
(pChim11)
AvaIII
BamHI
Tc^R
SalI

Fig. 12.

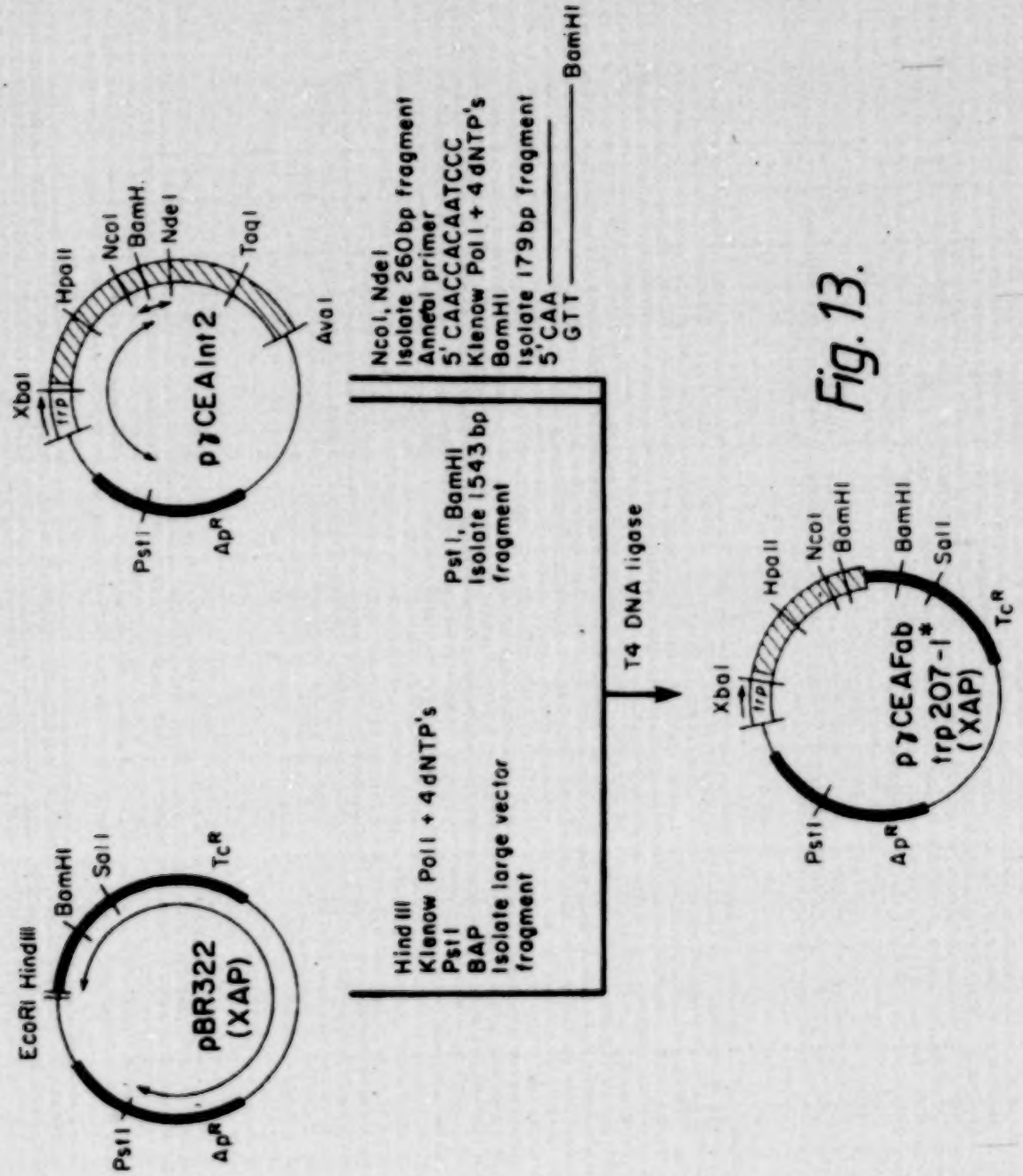
EcoRI HindIII
BamHI
SalI
TcR
pBR322
(XAP)
PstI
ApR
XbaI
trp
HpaII
NcoI
BamH.
NdeI
TaqI
AvaI
p7CEAInt2
PstI
ApR
HindIII
Klenow PolI + 4 dNTP's
PstI
BAP
Isolate large vector fragment
PstI, BamHI
Isolate 1543 bp fragment
NcoI, NdeI
Isolate 260bp fragment
Anneal primer
5' CAACCACAATCCC
Klenow PolI + 4 dNTP's
BamHI
Isolate 179 bp fragment
5'CAA
GTT
BamHI
T4 DNA ligase
XbaI
trp
HpaII
NcoI
BamHI
BamHI
SalI
TcR
p7CEAFab
trp207-1*
(XAP)
PstI
ApR

Fig. 13.

# METHODS OF PRODUCING IMMUNOGLOBULINS, VECTORS AND TRANSFORMED HOST CELLS FOR USE THEREIN

## CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 06/483,457, filed Apr. 8, 1983, now U.S. Pat. No. 4,816,567, issued Mar. 28, 1989.

## BACKGROUND OF THE INVENTION

This invention relates to the field of immunoglobulin production and to modification of naturally occurring immunoglobulin amino acid sequences. Specifically, the invention relates to using recombinant techniques to produce both immunoglobulins which are analogous to those normally found in vertebrate systems and to take advantage of these gene modification techniques to construct chimeric or other modified forms.

A. Immunoglobulins and Antibodies

Antibodies are specific immunoglobulin polypeptides produced by the vertebrate immune system in response to challenge by foreign proteins, glycoproteins, cells, or other antigenic foreign substances. The sequence of events which permits the organism to overcome invasion by foreign cells or to rid the system of foreign substances is at least partially understood. An important part of this process is the manufacture of antibodies which bind specifically to a particular foreign substance. The binding specificity of such polypeptides to a particular antigen is highly refined, and the multitude of specificities capable of being generated by the individual vertebrate is remarkable in its complexity and variability. Thousands of antigens are capable of eliciting responses, each almost exclusively directed to the particular antigen which elicited it.

Immunoglobulins include both antibodies, as above described, and analogous protein substances which lack antigen specificity. The latter are produced at low levels by the lymph system and in increased levels by myelomas.

A.1 Source and Utility

Two major sources of vertebrate antibodies are presently utilized—generation in situ by the mammalian B lymphocytes and in cell culture by B-cell hybrids. Antibodies are made in situ as a result of the differentiation of immature B lymphocytes into plasma cells, which occurs in response to stimulation by specific antigens. In the undifferentiated B cell, the portions of DNA coding for the various regions on the immunoglobulin chains are separated in the genomic DNA. The sequences are reassembled sequentially prior to transcription. A review of this process has been given by Gough, *Trends in Biochem Sci*, 6: 203 (1981). The resulting rearranged genome is capable of expression in the mature B lymphocyte to produce the desired antibody. Even when only a single antigen is introduced into the sphere of the immune system for a particular mammal, however, a uniform population of antibodies does not result. The in situ immune response to any particular antigen is defined by the mosaic of responses to the various determinants which are present on the antigen. Each subset of homologous antibody is contributed by a single population of B-cells—hence in situ generation of antibodies is "polyclonal".

This limited but inherent heterogeneity has been overcome in numerous particular cases by use of hybridoma technology to create "monoclonal" antibodies (Kohler, et al., *Eur J. Immunol*., 6: 511 (1976)). In this process, splenocytes



or lymphocytes from a mammal which has been injected with antigen are fused with a tumor cell line, thus producing hybrid cells or "hybridomas" which are both immortal and capable of producing the genetically coded antibody of the B cell. The hybrids thus formed we segregated into single genetic strains by selection, dilution, and regrowth, and each strain thus represents a single genetic line. They therefore produce immunoreactive antibodies against a desired antigen which are assured to be homogenous, and which antibodies, referencing their pure genetic parentage, are called "monoclonal". Hybridoma technology has to this time been focused largely on the fusion of murine lines, but human-human hybridomas (Olsson, L. et al., *Proc. Natl. Acad. Sci. (USA)*, 77: 5429 (1980)); human-murine hybridomas (Schlom, J., et al. (ibid) 77: 6841 (1980)) and several other xenogenic hybrid combinations have been prepared as well. Alternatively, primary, antibody producing, B cells have been immortalized in vitro by transformation with viral DNA.

Polyclonal, or, much more preferably monoclonal, antibodies have a variety of useful properties similar to those of the present invention. For example, they can be used as specific immunoprecipitating reagents to detect the presence of the antigen which elicited the initial processing of the B cell genome by coupling this antigen-antibody reaction with suitable detection techniques such as labeling with radioisotopes or with enzymes capable of assay (RIA, EMIT, and ELISA). Antibodies are thus the foundation of immuno diagnostic tests for many antigenic substances. In another important use, antibodies can be directly injected into subjects suffering from an attack by a substance or organism containing the antigen in question to combat this attack. This process is currently in its experimental stages, but its potential is clearly seen. Third, whole body diagnosis and treatment is made possible because injected antibodies are directed to specific target disease tissues, and thus can be used either to determine the presence of the disease by carrying with them a suitable label, or to attack the diseased tissue by carrying a suitable drug.

Monoclonal antibodies produced by hybridomas, while theoretically effective as suggested above and clearly preferable to polyclonal antibodies because of their specificity, suffer from certain disadvantages. First, they tend to be contaminated with other proteins and cellular materials of hybridoma, (and, therefore, mammalian) origin. These cells contain additional materials, notably nucleic acid fragments, but protein fragments as well, which are capable of enhancing, causing, or mediating carcinogic responses. Second, hybridoma lines producing monoclonal antibodies tend to be unstable and may alter the structure of antibody produced or stop producing antibody altogether (Kohler, G., et al. *Proc. Natl. Acad. Sci (USA)* 77: 2197 (1980); Morrison, S. L., *J. Immunol*. 123: 793 (1979)). The cell line genome appears to alter itself in response to stimuli whose nature is not currently known, and this alteration may result in production of incorrect sequences. Third, both hybridoma and B cells inevitably produce certain antibodies in glycosylated form (Melchers, F., *Biochemistry*, 10: 653 (1971)) which, under some circumstances, may be undesirable. Fourth, production of both monoclonal and polyclonal antibodies is relatively expensive. Fifth, and perhaps most important, production by current techniques (either by hybridoma or by B cell response) does not permit manipulation of the genome so as to produce antibodies with more effective design components than those normally elicited in response to antigens from the mature B cell in situ. The antibodies of the present invention do not suffer from the

foregoing drawbacks, and, furthermore, offer the opportunity to provide molecules of superior design.

Even those immunoglobulins which lack the specificity of antibodies are useful, although over a smaller spectrum of potential uses than the antibodies themselves. In presently understood applications, such immunoglobulins are helpful in proteins replacement therapy for globulin related anemia. In this context, an inability to bind to antigen is in fact helpful, as the therapeutic value of these proteins would be impaired by such functionality. At present, such non-specific antibodies are derivable in quantity only from myeloma cell cultures suitably induced. The present invention offers an alternative, more economical source. It also offers the opportunity of canceling out specificity by manipulating the four chains of the tetramer separately.

A.2 General Structure Characteristics

The basic immunoglobin structural unit in vertebrate systems is now well understood (Edelman, G. M., *Ann. N.Y. Acad. Sci.*, 190: 5 (1971)). The units are composed of two identical light polypeptide chains of molecular weight approximately 23,000 daltons, and two identical heavy chains of molecular weight 53,000–70,000. The four chains are joined by disulfide bonds in a "Y" configuration wherein the light chains bracket-the heavy-chains starting at the mouth of the Y and continuing through the divergent region as shown in FIG. 1. The "branch" portion, as there indicated, is designated the Fab region. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, with some subclasses among them, and the nature of this chain, as it has a long constant region, determines the "class"of the antibody as IgG, IgM, IgA, IgD, or IgE. Light chains are classified-as either kappa or lambda. Each heavy chain class can be prepared with either kappa or lambda light chain. The light and heavy chains are covalently bonded to each other, and the "tail" portions of the two heavy chains are bonded to each other by covalent disulfide linkages when the immunoglobulins are generated either by hybridomas or by B cells. However, if non-covalent association of the chains can be effected in the correct geometry, the aggregate will still be capable of reaction with antigen, or of utility as a protein supplement as a non-specific immunoglobulin.

The amino acid sequence runs from the N-terminal end at the top of the Y to the C-terminal end at the bottom of each chain. At the N-terminal end is a variable region which is specific for the antigen which elicited it, and is approximately 100 amino acids in length, there being slight variations between light and heavy chain and from antibody to antibody. The variable region is linked in each chain to a constant region which extends the remaining length of the chain. Linkage is seen, at the genomic level, as occurring through a linking sequence known currently as the "J" region in the light chain gene, which encodes about 12 amino acids, and as a combination of "D" region and "J" region in the heavy chain gene, which together encode approximately 25 amino acids.

The remaining portions of the chain are referred to as constant regions and within a particular class do not to vary with the specificity of the antibody (i.e., the antigen eliciting it).

As stated above, there are five known major classes of constant regions which determine the class of the immunoglobulin molecule (IgG, IgM, IgA, IgD, and IgE corresponding to $\gamma$, $\mu$, $\alpha$, $\delta$, and $\epsilon$ heavy chain constant regions). The constant region or class determines subsequent effector function of the antibody, including activation of complement (Kabat, E. A., *Structural Concepts in Immunology and Immunochemistry*, 2nd Ed., p. 413–436, Holt, Rinehart Winston (1976)), and other cellular responses (Andrews, D. W., et al., *Clinical Immunobiology* pp 1–18, W. B. Sanders (1980); Kohl, S., et al., *Immunology*, 48: 187 (1983)); while the variable region determines the antigen with which it will react.

B. Recombinant DNA Technology

Recombinant DNA technology has reached sufficient sophistication that it includes a repertoire of techniques for cloning and expression of gene sequences. Various DNA sequences can be recombined with some facility, creating new DNA entities capable of producing heterologous protein product in transformed microbes and cell cultures. The general means and methods for the in vitro ligation of various blunt ended or "sticky" ended fragments of DNA, for producing expression vectors, and for transforming organisms are now in hand.

DNA recombination of the essential elements (i.e., an origin of replication, one or more phenotypic selection characteristics, expression control sequence, heterologous gene insert and remainder vector) generally is performed outside the host cell. The resulting recombinant replicable expression vector, or plasmid, is introduced into cells by transformation and large quantities of the recombinant vehicle is obtained by growing the transformants. Where the gene is properly inserted with reference to portions which govern the transcription and translation of the encoded DNA message, the resulting expression vector is useful to produce the polypeptide sequence for which the inserted gene codes, a process referred to as "expression." The resulting product may be obtained by lysis, if necessary, of the host cell and recovery of the product by appropriate purifications from other proteins.

In practice, the use of recombinant DNA technology can express entirely heterologous polypeptides—so-called direct expression—or alternatively may express a heterologous polypeptide fused to a portion of the amino acid sequence of a homologous polypeptide. In the latter cases, the intended bioactive product is sometimes rendered bioinactive within the fused, homologous/heterologous polypeptide until it is cleaved in an extracellular environment.

The art of maintaining cell or tissue cultures as well as microbial systems for studying genetics and cell physiology is well established. Means and methods are available for maintaining permanent cell lines, prepared by successive serial transfers from isolated cells. For use in research, such cell lines are maintained on a solid support in liquid medium, or by growth in suspension containing support nutriments. Scale-up for large preparations seems to pose only mechanical problems.

## SUMMARY OF THE INVENTION

The invention relates to antibodies and to non-specific immunoglobulins (NSIs) formed by recombinant techniques using suitable host cell cultures. These antibodies and NSIs can be readily prepared in pure "monoclonal" form. They can be manipulated at the genomic level to produce chimeras of variants which draw their homology from species which differ from each other. They can also be manipulated at the protein level, since all four chains do not need to be produced by the same cell. Thus, there are a number of "types" of immunoglobulins encompassed by the invention.

First, immunoglobulins, particularly antibodies, are produced using recombinant techniques which mimic the amino acid sequence of naturally occurring antibodies produced by either mammalian B cells in situ, or by B cells fused with suitable immortalizing tumor lines, i.e., hybridomas.

Second, the methods of this invention produce, and the invention is directed to, immunoglobulins which comprise polypeptides not hitherto found associated with each other in nature. Such reassembly is particularly useful in producing "hybrid" antibodies capable of binding more than one antigen; and in producing "composite" immunoglobulins wherein heavy and light chains of different origins essentially damp out specificity. Third, by genetic manipulation, "chimeric" antibodies can be formed wherein, for example, the variable regions correspond to the amino acid sequence from one mammalian model system, whereas the constant region mimics the amino acid sequence of another. Again, the derivation of these two mimicked sequences may be from different species. Fourth, also by genetic manipulation, "altered" antibodies with improved specificity and other characteristics can be formed.

Two other types of immunoglobulin-like moieties may be produced: "univalent" antibodies, which are useful as homing carriers to target tissues, and "Fab proteins" which include only the "Fab" region of an immunoglobulin molecule i.e., the branches of the "Y". These univalent antibodies and Fab fragments may also be "mammalian" i.e., mimic mammalian amino acid sequences; novel assemblies of mammalian chains, or chimeric, where for example, the constant and variable sequence patterns may be of different origin. Finally, either the light chain or heavy chain alone, or portions, thereof, produced by recombinant techniques are included in the invention and may be mammalian or chimeric.

In other aspects, the invention is directed to DNA which encodes the aforementioned NSIs, antibodies, and portions thereof, as well as expression vectors or plasmids capable of effecting the production of such immunoglobulins in suitable host cells. It includes the host cells and cell cultures which result from transformation with these vectors. Finally, the invention is directed to methods of producing these NSIs and antibodies, and the DNA sequences, plasmids, and transformed cells intermediate to them.

## BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a representation of the general structure of immunoglobulins.

FIGS. **2A–B** shows the detailed sequence of the cDNA insert of pK17G4 which encodes kappa anti CEA chain.

FIG. **3** shows the coding sequence of the fragment shown in FIG. **2**, along with the corresponding amino acid sequence.

FIGS. **4A–C** shows the combined detailed sequence of the cDNA inserts of pγ298 and pγ11 which encode gamma anti CEA chain.

FIGS. **5A–B** shows the corresponding amino acid sequence encoded by the fragment in FIG. **4**.

FIGS. **6** and **7** outline the construction of expression vectors for kappa and gamma anti-CEA chains respectively.

FIGS. **8A**, **8B**, and **8C** show the results of sizing gels run on, extracts of *E. coli* expressing the genes for gamma chain, kappa chain, and both kappa and gamma chains respectively.

FIG. **9** shows the results of western blots of extracts of cells transformed as those in FIGS. **8**.

FIG. **10** shows a standard curve for ELISA assay of anti CEA activity.

FIGS. **11** and **12** show the construction of a plasmid for expression of the gene encoding a chimeric heavy chain.

FIG. **13** shows the construction of a plasmid for expression of the gene encoding the Fab region of heavy chain.

## DETAILED DESCRIPTION

### A. Definitions

As used herein, "antibodies" refers to tetramers or aggregates thereof which have specific immunoreactive activity, comprising light and heavy chains usually aggregated in the "Y" configuration of FIG. **1**, with or without covalent linkage between them; "immunoglobulins" refers to such assemblies whether or not specific immunoreactive activity is a property. "Non-specific immunoglobulin" ("NSI") means those immunoglobulins which do not possess specificity—i.e., those which are not antibodies.

"Mammalian antibodies" refers to antibodies wherein the amino acid sequences of the chains are homologous with those sequences found in antibodies produced by mammalian systems, either in situ, or in hybridomas. These antibodies mimic antibodies which are otherwise capable of being generated, although in impure form, in these traditional systems.

"Hybrid antibodies" refers to antibodies wherein chains are separately homologous with referenced mammalian antibody chains and represent novel assemblies of them, so that two different antigens are precipitable by the tetramer. In hybrid antibodies, one pair of heavy and light chain is homologous to antibodies raised against one antigen, while the other pair of heavy and light chain is homologous to those raised against another antigen. This results in the property of "divalence" i.e., ability to bind two antigens simultaneously. Such hybrids may, of course, also be formed using chimeric chains, as set forth below.

"Composite" immunoglobulins means those wherein the heavy and light chains mimic those of different species origins or specificities, and the resultant is thus likely to be a non-specific immunoglobulin (NSI), i.e.—lacking in antibody character.

"Chimeric antibodies" refers to those antibodies wherein one portion of each of the amino acid sequences of heavy and light chains is homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular class, while the remaining segment of the chains is homologous to corresponding sequences in another. Typically, in these chimeric antibodies, the variable region of both light and heavy chains mimics the variable regions of antibodies derived from one species of mammals while the constant portions are homologous to the sequences in antibodies derived from another. One clear advantage to such chimeric forms is that, for example, the variable regions can conveniently be derived from presently known sources using readily available hybridomas or B cells from non human host organisms in combination with constant regions derived from, for example, human cell preparations. While the variable region has the advantage of ease of preparation, and the specificity is not affected by its source, the constant region being human, is less likely to elicit an immune response from a human subject when the antibodies are injected than would the constant region from a non-human source.

However, the definition is not limited to this particular example. It includes any antibody in which either or both of the heavy or light chains are composed of combinations of sequences mimicking the sequences in antibodies of different sources, whether these sources be differing classes, differing antigen responses, or differing species of origin and whether or not the fusion point is At the variable constant boundary. Thus, it is possible to produce antibodies in which neither the constant nor the variable region mimic known antibody sequences. It then becomes possible, for example, to construct antibodies whose variable region has a higher

specific affinity for a particular antigen, or whose constant region can elicit enhanced complement fixation or to make other improvements in properties possessed by a particular constant region.

"Altered antibodies" means antibodies wherein the amino acid sequence has been varied from that of a mammalian or other vertebrate antibody. Because of the relevance of recombinant DNA techniques to this invention, one need not be confined to the sequences of amino acids found in natural antibodies; antibodies can be redesigned to obtain desired characteristics. The possible variations are many and range from the changing of just one or a few amino acids to the complete redesign of, for example, the constant region. Changes in the constant region will, in general, be made in order to improve the cellular process characteristics, such as complement fixation, interaction with membranes, and other effector functions. Changes in the variable region will be made in order to improve the antigen binding characteristics. The antibody can also be engineered so as to aid the specific delivery of a toxic agent according to the "magic bullet" concept. Alterations, can be made by standard recombinant techniques and also by oligonucleotide-directed mutagenesis techniques (Dalbadie-McFarland, et al *Proc. Natl. Acad. Sci.* (*USA*), 79:6,409 (1982)).

"Univalent antibodies" refers to aggregations which comprise a heavy chain light chain dimer bound to the Fc (or stem) region of a second heavy chain. Such antibodies are specific for antigen but have the additional desirable property of targeting tissues with specific antigenic surfaces, without causing its antigenic effectiveness to be impaired—i.e., there is no antigenic modulation. This phenomenon and the property of univalent antibodies in this regard is set forth in Glennie, M. J., et al., *Nature*, 295: 712 (1982). Univalent antibodies have heretofore been formed by proteolysis.

"Fab" region refers to those portions of the chains which are roughly equivalent, or analogous, to the sequences which comprise the Y branch portions of the heavy chain and to the light chain in its entirety, and which collectively (in aggregates) have been shown to exhibit antibody activity. "Fab protein", which protein is one of the aspects of the invention, includes aggregates of one heavy and one light chain (commonly known as Fab'), as well as tetramers which correspond to the two branch segments of the antibody Y, (commonly known as $F(ab)_2$), whether any of the above are covalently or non-covalently aggregated, so long as the aggregation is capable of selectively reacting with a particular antigen or antigen family. Fab antibodies have, as have univalent ones, been formed heretofore by proteolysis, and share the property of not eliciting antigen modulation on target tissues. However, as they lack the "effector" Fc: portion they cannot effect, for example, lysis of the target cell by macrophages.

"Fab protein" has similar subsets according to the definition of the present invention as does the general term "antibodies" or "immunoglobulins". Thus, "mammalian" Fab protein, "hybrid" Fab protein "chimeric" Fab and "altered" Fab protein are defined analogously to the corresponding definitions set forth in the previous paragraphs for the various types of antibodies.

Individual heavy or light chains may of course be "mammalian", "chimeric" or "altered" in accordance with the above. As will become apparent from the detailed description of the invention, it is possible, using the techniques disclosed to prepare other combinations of the four-peptide chain aggregates, besides those specifically defined, such as hybrid antibodies containing chimeric light and mammalian heavy chains, hybrid Fab proteins containing chimeric Fab proteins of heavy chains associated with mammalian light chains, and so forth.

"Expression vector" includes vectors which are capable of expressing DNA sequences contained therein, i.e., the coding sequences are operably linked to other sequences capable of effecting their expression. It is implied, although not always explicitly stated, that these expression vectors must be replicable in the host organisms either as episomes or as an integral part of the chromosomal DNA. Clearly a lack of replicability would render them effectively inoperable. A useful, but not a necessary, element of an effective expression vector is a marker encoding sequence—i.e. a sequence encoding a protein which results in a phenotypic property (e.g. tetracycline resistance) of the cells containing the protein which permits those cells to be readily identified. In sum, "expression vector" is given a functional definition, and any DNA sequence which is capable of effecting expression of a specified contained DNA code is included in this term, as it is applied to the specified sequence. As at present, such vectors are frequently in the form of plasmids, thus "plasmid" and "expression vector" are often used interchangeably. However, the invention is intended to include such other forms of expression vectors which serve equivalent functions and which may, from time to time become known in the art.

"Recombinant host cells" refers to cells which have been transformed with vectors constructed using recombinant DNA techniques. As defined herein, the antibody or modification thereof produced by a recombinant host cell is by virtue of this transformation, rather than in such lesser amounts, or more commonly, in such less than detectable amounts, as would be produced by the untransformed host.

In descriptions of processes for isolation of antibodies from recombinant hosts, the terms "cell" and "cell culture" are used interchangeably to denote the source of antibody unless it is clearly specified otherwise. In other words, recovery of antibody from the "cells" may mean either from spun down whole cells, or from the cell culture containing both the medium and the suspended cells.

B. Host Cell Cultures and Vectors

The vectors and methods disclosed herein are suitable for use in host cells over a wide range of prokaryotic and eukaryotic organisms.

In general, of course, prokaryotes are preferred for cloning of DNA sequences in constructing the vectors useful in the invention. For example, *E. coli* K12 strain 294 (ATCC No. 31446) is particularly useful. Other microbial strains which may be used include *E. coli* strains such as *E. coli* B, and *E. coli* X1776 (ATTC No. 31537). These examples are, of course, intended to be illustrative rather than limiting.

Prokaryotes may also be used for expression. The aforementioned strains, as well as *E. coli* W3110 ($F^-$, $\lambda^-$, prototrophic, ATTC No. 27325), bacilli such as *Bacillus subtilus*, and other enterobacteriaceae such as *Salmonella typhimurium* or *Serratia marcesans*, and various Pseudomonas species may be used.

In general, plasmid vectors containing replicon and control sequences which are derived from species compatible with the host cell are used in connection with these hosts. The vector ordinarily carries a replication site, as well as marking sequences which are capable of providing phenotypic selection in transformed cells. For example, *E. coli* is typically transformed using pBR322, a plasmid derived from an *E. coli* species (Bolivar, et al., *Gene* 2: 95 (1977)). PBR322 contains genes for ampicillin and tetracycline resistance and thus provides easy means for identifying transformed cells. The pBR322 plasmid, or other microbial

plasmid must also contain, or be modified to contain, promoters which can be used by the microbial organism for expression of its own proteins. Those promoters most commonly used in recombinant DNA construction include the β-lactamase (penicillinase) and lactose promoter systems Chang et al, *Nature* 275: 615 (1978); Itakura, et al, *Science* 198: 1056 (1977); (Goeddel et al, *Nature* 281: 544 (1979)) and a tryptophan (trp) promoter system (Goeddel, et al, *Nucleic kids Res.*, 8: 4057 (1980); EPO Appl Publ No. 0036776). While these are the most commonly used, other microbial promoters have been discovered and utilized., and details concerning their nucleotide sequences have been published, enabling a skilled worker to ligate them functionally with plasmid vectors (Siebenlist, et al, Cell 20: 269 (1980)).

In addition to prokaryates, eukaryotic microbes, such as yeast cultures may also be used. *Saccharomyces cerevisiae*, or common baker's yeast is the most commonly used among eukaryotic microorganisms, although a number of other strains are commonly available. For expression in Saccharomyces, the plasmid YRp7, for example, (Stinchcomb et al, *Nature*, 282: 39 (1979); Kingsman et al, *Gene*, 7: 141 (1979); Tschemper, et al, *Gene*, 10: 157 (1980)) is commonly used. This plasmid already contains the trp1 gene which provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example ATCC No. 44076 or PEP4-1 (Jones, *Genetics*, 85: 12 (1977)). The presence of the trp1 lesion as a characteristic of the yeast host cell genome then provides an effective environment for detecting transformation by growth in the absence of tryptophan.

Suitable promoting sequences in yeast vectors include the promoters for 3-phosphoglycerate kinase (Hitzeman, et al., *J. Biol. Chem.*, 255: 2073 (1980)) or other glycolytic enzymes (Hess, et al, *J. Adv. Enzyme Reg.*, 7: 149 (1968); Holland, et al, *Biochemistry*, 17: 4900 (1978)), such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase. In constructing suitable expression plasmids, the termination sequences associated with these genes are also ligated into the expression vector 3' of the sequence desired to be expressed to provide polyadenylation of the mRNA and termination. Other promoters, which have the additional advantage of transcription controlled by growth conditions are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, and the aforementioned glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization (Holland, ibid.). Any plasmid vector containing yeast-compatible promoter, origin of replication and termination sequences is suitable.

In addition to microorganisms cultures of cells derived from multicellular organisms may also be used as hosts. In principle, any such cell culture is workable, whether from vertebrate or invertebrate culture. However interest has been greatest in vertebrate cells, and propagation of vertebrate cells in culture (tissue culture) has become a routine procedure in recent years (*Tissue Culture*, Academic Press, Kruse and Patterson, editors (1973)). Examples of such useful host cell lines are VERO and HeLa cells, Chinese hamster ovary (CHO) cell lines, and W138, BHK, COS-7 and MDCK cell lines. Expression vectors for such cells ordinarily include (if necessary) an origin of replication, a promoter located in front of the gene to be expressed, along with any necessary ribosome binding sites, RNA splice sites, polyadenylation site, and transcriptional terminator sequences.

For use in mammalian cells, the control functions on the expression vectors are often provided by viral material. For example, commonly used promoters are derived from polyoma, Adenovirus 2, and most frequently Simian Virus 40 (SV40). The early and late promoters of SV40 virus are particularly useful because both are obtained easily from the virus as a fragment which also contains the SV40 viral origin of replication (Fiers, et al, *Nature*, 273: 113 (1978)) incorporated herein by reference. Smaller or larger SV40 fragments may also be used, provided there is included the approximately 250 bp sequence extending from the Hind III site toward the Bgl I site located in the viral origin of replication. Further, it is also possible, and often desirable, to utilize promoter or control sequences normally associated with the desired gene sequence, provided such control sequences are compatible with the host cell systems.

An origin of replication may be provided either by construction of the vector to include an exogenous origin, such as may be derived from SV40 or other viral (e.g. Polyoma, Adeno, VSV, BPV, etc.) source, or may be provided by the host cell chromosomal replication mechanism. If the vector is integrated into the host cell chromosome, the latter is often sufficient.

It will be understood that this invention, although described herein in terms of a preferred embodiment, should not be construed as limited to those host cells, vectors and expression systems exemplified.

C. Methods Employed

C.1 Transformation

If cells without formidable cell wall barriers are used as host cells, transfection is carried out by the calcium phosphate precipitation method as described by Graham and Van der Eb, *Virology*, 52: 546 (1978). However, other methods for introducing DNA into cells such as by nuclear injection or by protoplast fusion may also be used.

If prokaryotic cells or cells which contain substantial cell wall constructions are used, the preferred method of transfection is calcium treatment using calcium chloride as described by Cohen, F. N. et al *Proc. Natl. Acad. Sci. (USA)* 69: 2110 (1972).

C.2 Vector Construction

Construction of suitable vectors containing the desired coding and control sequences employ standard ligation techniques. Isolated plasmids or DNA fragments are cleaved, tailored, and religated in the form desired to form the plasmids required. The methods employed are not dependent on the DNA source, or intended host.

Cleavage is performed by treating with restriction enzyme (or enzymes) in suitable buffer. In general, about 1 μg plasmid or DNA fragments is used with about 1 unit of enzyme in about 20 μl of buffer solution. (Appropriate buffers and substrate amounts for particular restriction enzymes are specified by the manufacturer.) Incubation times of about 1 hour at 37° C. are workable. After incubations, protein is removed by extraction with phenol and chloroform, and the nucleic acid is recovered from the aqueous fraction by precipitation with ethanol.

If blunt ends are required, the preparation is treated for 15 minutes at 15° with 10 units of *E. coli* DNA Polymerase I (Klenow), phenol-chloroform extracted, and ethanol precipitated.

Size separation of the cleaved fragments is performed using 6 percent polyacrylamide gel described by Goeddel, D., et al, *Nucleic Acids Res.*, 8: 4057 (1980) incorporated herein by reference.

For ligation, approximately equimolar amounts of the desired components, suitably end tailored to provide correct matching are treated with about 10 units T4 DNA ligase per 0.5 μg DNA. (When cleaved vectors are used as components, it may be useful to prevent religation of the cleaved vector by pretreatment with bacterial alkaline phosphatase.)

In the examples described below correct ligations for plasmid construction are confirmed by transforming *E. coli* K12 strain 294 (ATCC 31446) with the ligation mixture. Successful transformants were selected by ampicillin or tetracycline resistance depending on the mode of plasmid construction. Plasmids from the transformants were then prepared, analyzed by restriction and/or sequenced by the method of Messing, et al, *Nucleic Acids Res.*, 9:309 (1981) or by the method of Maxam, et al, *Methods in Enzymology*, 65:499 (1980).

D. Outline of Procedures

D.1 Mammalian Antibodies

The first type of antibody which forms a part of this invention, and is prepared by the methods thereof, is "mammalian antibody"-one wherein the heavy and light chains mimic the amino acid sequences of an antibody otherwise produced by a mature mammalian B lymphocyte either in situ or when fused with an immortalized cell as part of a hybridoma culture. In outline, these antibodies are produced as follows:

Messenger RNA coding for heavy or light chain is isolated from a suitable source, either mature B cells or a hybridoma culture, employing standard techniques of RNA isolation, and the use of oligo-dT cellulose chromatography to segregate the poly-A mRNA. The poly-A mRNA may, further, be fractionated to obtain sequences of sufficient size to code for the amino acid sequences in the light or heavy chain of the desired antibody as the case may be.

A cDNA library is then prepared from the mixture of mRNA using a suitable primer, preferably a nucleic acid sequence which is characteristic of the desired cDNA. Such a primer may be hypothesized and synthesized based on the amino acid sequence of the antibody if the sequence is known. In the alternative cDNA from unfractionated poly-A mRNA from a cell line producing the desired antibody or poly-dT may also be used. The resulting cDNA is optionally size fractionated on polyacrylamide gel and then extended with, for example, dC residues for annealing with pBR322 or other suitable cloning vector which has been cleaved by a suitable restriction enzyme, such as Pst I, and extended with dG residues. Alternative means of forming cloning vectors containing the cDNA using other tails and other cloning vector remainder may, of course, also be used but the foregoing is a standard and preferable choice. A suitable host cell strain, typically *E. coli*, is transformed with the annealed cloning vectors, and the successful transformants identified by means of, for example, tetracycline resistance or other phenotypic characteristic residing on the cloning vector plasmid.

Successful transformants are picked and transferred to microtiter dishes or other support for further growth and preservation. Nitrocellulose filter imprints of these growing cultures are then probed with suitable nucleotide sequences containing bases known to be complementary to desired sequences in the cDNA. Several types of probe may be used, preferably synthetic single stranded DNA sequences labeled by kinasing with $ATP^{32}$. The cells fixed to the nitrocellulose filter are lysed, the DNA denatured, and then fixed before reaction with kinased probe. Clones which successfully hybridize are detected by contact with a photoplate, then plasmids from the growing colonies isolated and sequenced by means known in the art to verify that the desired portions of the gene are present.

The desired gene fragments are excised and tailored to assure appropriate reading frame with the control segments when inserted into suitable expression vectors. Typically, nucleotides are added to the 5' end to include a start signal and a suitably positioned restriction endonuclease site.

The tailored gene sequence is then positioned in a vector which contains a promoter in reading frame with the gene and compatible with the proposed host cell. A number of plasmids such as those described in U.S. patent application Ser. Nos. 307,473; 291,892; and 305,657 (EPO Publ. Nos. 0036776; 0048970 and 0051873) have been described which already contain the appropriate promoters, control sequences, ribosome binding sites, and transcription termination sites, as well as convenient markers.

In the present invention, the gene coding for the light chain and that coding for the heaving chain are recovered separately by the procedures outlined above. Thus then may be inserted into separate expression plasmids, or together in the same plasmid, so long as each is under suitable promoter and translation control.

The expression vectors constructed above are then used to transform suitable cells. The light and heavy chains may be transformed into separate cell cultures, either of the same or of differing species; separate plasmids for light and heavy chain may be used to co-transform a single cell culture, or, finally, a single expression plasmid containing both genes and capable of expressing the genes for both light and heavy chain may be transformed into a single cell culture.

Regardless of which of the three foregoing options is chosen, the cells are grown under conditions appropriate to the production of the desired protein. Such conditions are primarily mandated by the type of promoter and control systems used in the expression vector, rather than by the nature of the desired protein. The protein thus produced is then recovered from the cell culture by methods known in the art, but choice of which is necessarily dependent on the form in which the protein is expressed. For example, it is common for mature heterologous proteins expressed in *E. coli* to be deposited within the cells as insoluble particles which require cell lysis and solubilization in denaturant to permit recovery. On the other hand, proteins under proper synthesis circumstances, in yeast and bacterial strains, can be secreted into the medium (yeast and gram positive bacteria) or into the periplasmic space (gram negative bacteria) allowing recovery by less drastic procedures. Tissue culture cells as hosts also appear, in general, to permit reasonably facile recovery of heterologous proteins.

When heavy and light chain are coexpressed in the same host, the isolation procedure is designed so as to recover reconstituted antibody. This can be accomplished in vitro as described below, or might be possible in vivo in a microorganism which secretes the IgG chains out of the reducing environment of the cytoplasm. A more detailed description is given in D.2, below.

D.2 Chain Recombination Techniques

The ability of the method of the invention to produce heavy and light chains or portions thereof, in isolation from each other offers the opportunity to obtain unique and unprecedented assemblies of immunoglobulins, Fab regions, and univalent antibodies. Such preparations require the use of techniques to reassemble isolated chains. Such means are known in the art, and it is, thus, appropriate to review them here.

While single chain disulfide bond containing proteins have been reduced and reoxidized to regenerate in high yield

native structure and activity (Freedman, R. B., et al. In *Enzymology of Post Translational Modification of Proteins,* I: 157–212 (1980) Academic Press, NY.), proteins which consist of discontinuous polypeptide chains held together by disulfide bonds are more difficult to reconstruct in vitro after reductive cleavage. Insulin, a cameo case, has received much experimental attention over the years, and can now be reconstructed so efficiently that an industrial process has been built around it (Chance, R. E., et al., In *Peptides: Proceedings of the Seventh Annual American Peptide Symposium* (Rich, D. H. and Gross. E., eds.) 721–728, Pierce Chemical Co., Rockford, Ill. (1981)).

Immunoglobulin has proved a more difficult problem than insulin. The tetramer is stabilized intra and intermolecularly by 15 or more disulfide bonds. It has been possible to recombine heavy and light chains, disrupted by cleavage of only the interchain disulfides, to regain antibody activity even without restoration of the inter-chain disulfides (Edelman, G. M., et al., *Proc. Natl. Acad. Sci. (USA)* 50: 753 (1963)). In addition, active fragments of IgG formed by proteolysis (Fab fragments of ~50,000 MW) can be split into their fully reduced heavy chain and light chain components and fairly efficiently reconstructed to give active antibody (Haber, E., *Proc. Natl. Acad. Sci. (USA)* 52: 1099 (1964); Whitney, P. L., et al., *Proc. Natl. Acad. Sci. (USA)* 53: 524 (1965)). Attempts to reconstitute active antibody from fully reduced native IgG have been largely unsuccessful, presumably due to insolubility of the reduced chains and of side products or intermediates in the refolding pathway (see discussion in Freedman, M. H., et al., *J. Biol. Chem.* 241: 5225 (1966)). If, however, the immunoglobulin is randomly modified by polyalanylation of its lysines before complete reduction, the separated chains have the ability to recover antigen-combining activity upon reoxidation (ibid).

A particularly suitable method for immunoglobulin reconstitution is derivable from the now classical insulin recombination studies, wherein starting material was prepared by oxidative sulfitolysis, thus generating thiol-labile S-sulfonate groups at all cysteines in the protein, non-reductively breaking disulfides (Chance et al. (supra)). Oxidative sulfitolysis is a mild disulfide cleavage reaction (Means, G. E., et al., *Chemical Modification of Proteins,* Holden-Day, San Francisco (1971)) which is sometimes more gentle than reduction, and which generates derivatives which are stable until exposed to mild reducing agent at which time disulfide reformation can occur via thiol-disulfide interchange. In the present invention the heavy and light chain S-sulfonates generated by oxidative sulfitolysis were reconstituted utilizing both air oxidation and thiol-disulfide interchange to drive disulfide bond formation. The general procedure is set forth in detail in U.S. Ser. No. 452,187, filed Dec. 22, 1982 (EPO Appln. No. 83.307840.5), incorporated herein by reference.

D.3 Variants Permitted by Recombinant Technology

Using the techniques described in paragraphs D.1 and D.2, additional operations which were utilized to gain efficient production of mammalian antibody can be varied in quite straightforward and simple ways to produce a great variety of modifications of this basic antibody form. These variations are inherent in the use of recombinant technology, which permits modification at a genetic level of amino acid sequences in normally encountered mammalian immunoglobulin chains, and the great power of this approach lies in its ability to achieve these variations, as well as in its potential for economic and specific production of desired scarce, and often contaminated, molecules. The variations also inhere in the ability to isolate production of individual chains, and thus create novel assemblies.

Briefly, since genetic manipulations permit reconstruction of genomic material in the process of construction of expression vectors, such reconstruction can be manipulated to produce new coding sequences for the components of "natural" antibodies or immunoglobulins. As discussed in further detail below, the coding sequence for a mammalian heavy chain may not be derived entirely from a single source or single species, but portions of a sequence can be recovered by the techniques described in D.1 from differing pools of mRNA, such as murine-murine hybridomas, human-murine hybridomas, or B cells differentiated in response to a series of antigen challenges. The desired portions of the sequences in each case can be recovered using the probe and analysis techniques described in D.1, and recombined in an expression vector using the same ligation procedures as would be employed for portions of the same model sequence. Such chimeric chains can be constructed of any desired length; hence, for example, a complete heavy chain can be constructed, or only sequence for the Fab region thereof.

The additional area of flexibility which arises from the use of recombinant techniques results from the power to produce heavy and light chains or fragments thereof in separate cultures or of unique combinations of heavy and light chain in the same culture, and to prevent reconstitution of the antibody or immunoglobulin aggregation until the suitable components are assembled. Thus, while normal antibody production results automatically in the formation of "mammalian antibodies" because the light and heavy chain portions are constructed in response to a particular determinant in the same cell, the methods of the present invention present the opportunity to assemble entirely new mixtures. Somewhat limited quantities of "hybrid" antibodies have been produced by "quadromas" i.e., fusions of two hybridoma cell cultures which permit random assemblies of the heavy and light chains so produced.

The present invention permits a more controlled assembly of desired chains, either by mixing the desired chains in vitro, or by transforming the same culture with the coding sequences for the desired chains.

D.4 Composite Immunoglobulins

The foregoing procedure, which describes in detail the recombinant production of mammalian antibodies is employed with some modifications to construct the remaining types of antibodies or NSIs encompassed by the present invention. To prepare the particular embodiment of composite non-specific immunoglobulin wherein the homology of the chains corresponds to the sequences of immunoglobulins of different specificities, it is of course, only necessary to prepare the heavy and light chains in separate cultures and reassemble them as desired.

For example, in order to make an anti-CEA light chain/antihepatitis heavy chain composite antibody, a suitable source for the mRNA used as a template for the light chain clone would comprise, for instance, the anti CEA producing cell line of paragraph E.1. The mRNA corresponding to heavy chain would be derived from B cells raised in response to hepatitis infection or from hybridoma in which the B cell was of this origin. It is clear that such composites can be assembled using the methods of the invention almost at will, and are limited only by available sources of mRNA suitable for use as templates for the respective chains. All other features of the process are similar to those described above.

D.5 Hybrid Antibodies

Hybrid antibodies are particularly useful as they are capable of simultaneous reaction with more than one antigen. Pairs of heavy and light chains corresponding to chains

of antibodies for different antigens, such as those set forth in paragraph D.4 are prepared in four separate cultures, thus preventing premature assembly of the tetramer. Subsequent mixing of the four separately prepared peptides then permits assembly into the desired tetramers. While random aggregation may lead to the formation of considerable undesired product, that portion of the product in which homologous light and heavy chains are bound to each other and mismatched to another pair gives the desired hybrid antibody.

D.6 Chimeric Antibodies

For construction of chimeric antibodies (wherein, for example, the variable sequences are separately derived from the constant sequences) the procedures of paragraph C.1 and D.2 are again applicable with appropriate additions and modifications. A preferred procedure is to recover desired portions of the genes encoding for parts of the heavy and light chains from suitable, differing, sources and then to religate these fragments using restriction endonucleases to reconstruct the gene coding for each chain.

For example, in a particularly preferred chimeric construction, portions of the heavy chain gene and of the light chain gene which encode the variable sequences of antibodies produced by a murine hybridoma culture are recovered and closed from this culture and gene fragments encoding the constant regions of the heavy and light chains for human antibodies recovered and cloned from, for example, human myeloma cells. Suitable restriction enzymes may then be used to ligate the variable portions of the mouse gene to the constant regions of the human gene for each of the two chains. The chimeric chains are produced as set forth in D.1, aggregated as set forth in D.2 and used in the same manner as the non-chimeric forms. Of course, any splice point in the chains can be chosen.

D.7 Altered Antibodies

Altered antibodies present, in essence, an extension of chimeric ones. Again, the techniques of D.1 and D.2 are applicable; however, rather than splicing portions of the chain(s), suitable amino acid alterations, deletions or additions are made using available techniques such as mutagenesis (supra). For example, genes which encode antibodies having diminished complement fixation properties, or which have enhanced metal binding capacities are prepared using such techniques. The latter type may, for example, take advantage of the known gene sequence encoding metallothionein II (Karin, M., et al., *Nature*, 299: 797 (1982)). The chelating properties of this molecular fragment are useful in carrying heavy metals to tumor sites as an aid in tumor imaging (Scheinberg, D. A., et al., *Science*, 215: 19 (1982).

D.8 Univalent Antibodies

In another preferred embodiment, antibodies are formed which comprise one heavy and light chain pair coupled with the Fc region of a third (heavy) chain. These antibodies have a particularly useful property. They can, like ordinary antibodies, be used to target antigenic surfaces of tissues, such as tumors, but, unlike ordinary antibodies, they do not cause the antigenic surfaces of the target tissue to retreat and become non-receptive. Ordinary antibody use results in aggregation and subsequent inactivation, for several hours, of such surface antigens.

The method of construction of univalent antibodies is a straightforward application of the invention. The gene for heavy chain of the desired Fc region is cleaved by restriction enzymes, and only that portion coding for the desired Fc region expressed. This portion is then bound using the technique of D.2 to separately produced heavy chain the desired pairs separated from heavy heavy and Fc Fc combinations, and separately produced light chain added. Pre-binding of the two heavy chain portions thus diminishes the probability of formation of ordinary antibody.

D.9 Fab Protein

Similarly, it is not necessary to include the entire gene for the heavy chain portion. All of the aforementioned variations can be superimposed on a procedure for Fab protein production and the overall procedure differs only in that the portion of the heavy chain coding for the amino terminal **220** amino acids is employed in the appropriate expression vector.

E. Specific Examples of Preferred Embodiments

The invention has been described above in general terms and there follow several specific examples of embodiments which set forth details of experimental procedure in producing the desired antibodies. Example E.1 sets forth the general procedure for preparing anti CEA antibody components, i.e. for a "mammalian antibody". Example E.3 sets forth the procedure for reconstitution and thus is applicable to preparation of mammalian, composite, hybrid and chimeric immunoglobulins, and Fab proteins and univalent antibodies. Example E.4 sets forth the procedure for tailoring the heavy or light chain so that the variable and constant regions may be derived from different sources. Example E.5 sets forth the method of obtaining a shortened heavy chain genome which permits the production of the Fab regions and, in an analogous manner, Fc region.

The examples set forth below are included for illustrative purposes and do not limit the scope of the invention.

E.1 Construction of Expression Vectors for Murine anti-CEA Antibody Chains and Peptide Synthesis

Carcinoembryonic antigen (CEA) is associated with the surface of certain tumor cells of human origin (Gold, P., et al., *J. Exp. Med.*, 122: 467 (1965)). Antibodies which bind to CEA (anti-CEA antibodies) are useful in early detection of these tumors (Van Nagell, T. R., et al., *Cancer Res.* 40: 502 (1980)), and have the potential for use in treatment of those human tumors which appear to support CEA at their surfaces. A mouse hybridoma cell line which secretes anti-CEA antibodies of the $IgG_1$ class, CEA.66-E3, has been prepared as described by Wagener, C, et al., *J. Immunol.* (in press) which is incorporated herein by reference, and was used as mRNA source. The production of anti CEA antibodies by this cell line was determined. The N-terminal sequences of the antibodies produced by these cells was compared with those of monoclonal anti CEA as follows. Purified IgG was treated with PCAse (Podell, D. N., et al., BBRC 81: 176 (1978)), and then dissociated in 6M guanidine hydrochloride, 10 mM 2-mercaptoethanol (1.0 mg of immunoglobulin, 5 min, 100° C. water bath). The dissociated chains were separated on a Waters Associates alkyl phenyl column using a linear gradient from 100 percent A (0.1 percent TFA-water) to 90 percent B (TFA/$H_2O$/MeCN 0.1/9.9/90) at a flow rate of 0.8 ml/min. Three major peaks were eluted and analyzed on SDS gels by silver staining. The first two peaks were pure light chain (MW 25,000 daltons), the third peak showed a (7:3) mixture of heavy and light chain. 1.2 nmoles of light chain were sequenced by the method of Shively, J. E., *Methods in Enzymology*, 79: 31 (1981), with an $NH_2$-terminal yield of 0.4 nmoles. A mixture of heavy and light chains (3 nmoles) was also sequenced, and sequence of light chain was deducted from the double sequence to yield the sequence of the heavy chain.

In the description which follows, isolation and expression of the genes for the heavy and light chains for anti CEA antibody produced by CEA.66-E3 are described. As the constant regions of these chains belong to the gamma and kappa families, respectively, "light chain" and "kappa

chain", and "heavy chain" and "gamma chain", respectively, are used interchangeably below.

E.1.1 Isolation of Messenger RNA for Anti CEA Light and Heavy (Kappa and Gamma) Chains

Total RNA from CEA.66-E3 cells was extracted essentially as reported by Lynch et al, *Virology*, 98: 251 (1979). Cells were pelleted by centrifugation and approximately 1 g portions of pellet resuspended in 10 ml of 10 mM NaCl, 10 mM Tris HCl (pH 7.4), 1.5 mM $MgCl_2$. The resuspended cells were lysed by addition of non-ionic detergent NP-40 to a final concentration of 1 percent, and nuclei removed by centrifugation. After addition of SDS (pH 7.4) to 1 percent final concentration, the supernatant was extracted twice with 3 ml portions of phenol (redistilled)/chloroform: isoamyl alcohol 25:1 at 4° C. The aqueous phase was made 0.2 M in NaCl and total RNA was precipitated by addition of two volumes of 100 percent ethanol and overnight storage at −20° C. After centrifugation, polyA mRNA was purified from total RNA by oligo-dT cellulose chromatography as described by Aviv and Leder, *Proc. Nat'l, Acad. Sci. (USA)*, 69: 1408 (19672), 142 μg of polyA mRNA was obtained from 1 g cells.

E.1.2 Preparation of *E. coli* Colony Library Containing Plasmids with Heavy and Light DNA Sequence Inserts

5 μg of the unfractionated polyA mRNA prepared in paragraph E.1.1 was used as template for oligo-dT primed preparation of double-stranded (ds) cDNA by standard procedures as described by Goeddel et al., *Nature* 281: 544 (1979) and Wickens et al., *J. Biol. Chem.* 253: 2483 (1978) incorporated herein by reference. The cDNA was size fractionated by 6 percent polyacrylamide gel electrophoresis and 124 ng of ds cDNA greater than 600 base pairs in length was recovered by electroelution. A 20 ng portion of ds cDNA was extended with deoxy C residues using terminal deoxynucleotidyl transferase as described in Chang et al., *Nature* 275: 617 (1978) incorporated herein by reference, and annealed with 200 ng of the plasmid pBR322 (Bolivar et al., *Gene* 2: 95 (1977)) which had been cleaved with Pst I and tailed with deoxy G. Each annealed mixture was then transformed into *E. coli* K12 strain 294 (ATCC No. 31446). Approximately 8500 ampicillin sensitive, tetracycline resistant transformants were obtained.

E.1.3 Preparation of Synthetic Probes

The 14mer, 5' GGTGGGAAGATGGA 3' complementary to the coding sequence of constant region for mouse MOPC21 kappa chain which begins 25 basepairs 3' of the variable region DNA sequence was used as kappa chain probe. A 15 mer, 5' GACCAGGCATCCCAG 3', complementary to a coding sequence located 72 basepairs 3' of the variable region DNA sequence for mouse MOPC21 gamma chain was used to probe gamma chain gene.

Both probes were synthesized by the phosphotriester method described in German Offenlegungschrift 2644432, incorporated herein by reference, and made radioactive by kinasing as follows: 250 ng of deoxyoligonucleotide were combined in 25 μl of 60 mM Tris HCl (pH 8), 10 mM $MgCl_2$, 15 mM beta-mercaptoethanol, and 100 μCi ($\gamma$-$^{32}$P) ATP (Amersham, 5000 Ci/mMole). 5 units of T4 polynucleotide kinase were added and the reduction was allowed to proceed at 37° C. for 30 minutes and terminated by addition of EDTA to 20 mM.

E.1.4 Screening of Colony Library for Kappa or Gamma Chain Sequences

~2000 colonies prepared as described in paragraph E.1.2 were individually inoculated into wells of microtitre dishes containing LB (Miller, Experiments in Molecular Genetics, p. 431–3, Cold Spring Harbor, Lab., Cold Spring Harbor, N.Y. (1972))+5 μg/ml tetracycline and stored at −20° C. after addition of DMSO to 7 percent. Individual colonies from this library were transferred to duplicate sets of Schleicher and Schuell BA85/20 nitrocellulose filters and grown on agar plates containing LB+5 μg/ml tetracycline. After ~10 hours growth at 37° C. the colony filters were transferred to agar plates containing LB+5 μg/ml tetracycline and 12.5 μg/ml chloramphenicol and reincubated overnight at 37° C. The DNA from each colony was then denatured and fixed to the filter by a modification of the Grunstein-Hogness procedure as described in Grunstein et al., *Proc. Natl. Acad. Sci. (USA)* 72: 3961 (1975), incorporated herein by reference. Each filter was floated for 3 minutes on 0.5 N NaOH, 1.5 M NaCl to lyse the colonies and denature the DNA then neutralized by floating for 15 minutes on 3 M NaCl, 0.5 M Tris HCl (pH 7.5). The filters were then floated for an additional 15 minutes on 2XSSC, and subsequently baked for 2 hours in an 80° C. vacuum oven. The filters were prehybridized for ~2 hours at room temperature in 0.9 M NaCl, 1X Denhardts, 100 mM Tris HCl (pH 7.5), 5 mM Na-EDTA, 1 mM ATP, 1 M sodium phosphate (dibasic), 1 mM sodium pyrophosphate, 0.5 percent NP-40, and 200 μg/ml *E. coli* t-RNA, and hybridized in the same solution overnight, essentially as described by Wallace et al. *Nucleic Acids Research* 9: 879 (1981) using ~$40\times10^6$ cpm of either the kinased kappa or gamma probe described above.

After extensive washing at 37° C. in 6X SSC, 0.1 percent SDS, the filters were exposed to Kodak XR-5 X-ray film with DuPont Lightning-Plus intensifying screens for 16–24 hours at −80° C. Approximately 20 colonies which hybridized with kappa chain probe and 20 which hybridized with gamma chain probe were characterized.

E.1.5 Characterization of Colonies which Hybridize to Kappa DNA Sequence Probe

Plasmid DNAs isolated from several different transformants which hybridized to kappa chain probe were cleaved with Pst I and fractionated by polyacrylamide gel electrophoresis (PAGE). This analysis demonstrated that a number of plasmid DNAs contained cDNA inserts large enough to encode full length kappa chain. The complete nucleotide sequence of the cDNA insert of one of these plasmids was determined by the dideoxynucleotide chain termination method as described by Smith, *Methods Enzymol.* 65, 560 (1980) incorporated herein by reference after subcloning restriction endonuclease cleavage fragments into M13 vectors (Messing et al., *Nucleic Acids Research* 9: 309 (1981). FIG. 2 shows the nucleotide sequence of the cDNA insert of pK17G4 and FIG. 3 shows the gene sequence with the corresponding amino acid sequence. Thus, the entire coding region of mouse anti-CEA kappa chain was isolated on this one large DNA fragment. The amino acid sequence of kappa chain, deduced from the nucleotide sequence of the pK17G4 cDNA insert, corresponds perfectly with the first 23 N-terminal amino acids of mature mouse anti-CEA kappa chain as determined by amino acid sequence analysis of purified mouse anti-CEA kappa chain. The coding region of pK17G4 contains 27 basepairs or 9 amino acids of the presequence and 642 basepairs or 214 amino acids of the mature protein. The mature unglycosylated protein (MW 24,553) has a variable region of 119 amino acids, including the J1 joining region of 12 amino acids, and a constant region of 107 amino acids. After the stop codon behind amino acids 215 begins 212 basepairs of 3' untranslated sequence up to the polyA addition. The kappa chain probe used to identify pK17G4 hybridizes to nucleotides 374–388 (FIG. 2).

E.1.6 Characterization of Colonies which Hybridize to Gamma 1 DNA Probe

Plasmid DNA isolated from several transformants positive for hybridization with the heavy chain gamma 1 probe was subjected to Pst I restriction endonuclease analysis as described in E.1.5. Plasmid DNAs demonstrating the largest cDNA insert fragments were selected for further study. Nucleotide sequence coding for mouse heavy (gamma-1) chain, shows an NcoI restriction endonuclease cleavage site near the junction between variable and constant region. Selected plasmid DNAs were digested with both PstI and NcoI and sized on polyacrylamide. This analysis allowed identification of a number of plasmid DNAs that contain NcoI restriction endonuclease sites, although none that demonstrate cDNA insert fragments large enough to encode the entire coding region of mouse anti-CEA heavy chain.

In one plasmid isolated, p γ298 the cDNA insert of about 1300 bp contains sequence information for the 5' untranslated region, the signal sequence and the N-terminal portion of heavy chain. Because pγ298 did not encode the C-terminal sequence for mouse anti-CEA gamma 1 chain, plasmid DNA was isolated from other colonies and screened with PstI and NcoI. The C-terminal region of the cDNA insert of pγ11 was sequence and shown to contain the stop codon, 3' untranslated sequence and that portion of the coding sequence missing from p γ298.

FIG. **4** presents the entire nucleotide sequence of mouse anti-CEA heavy chain (as determined by the dideoxynucleotide chain termination method of Smith, *Methods Enzymol.*, 65: 560 (1980)) and FIG. **5** includes the translated sequence.

The amino acid sequence of gamma 1 (heavy chain) deduced from the nucleotide sequence of the pγ298 cDNA insert corresponds perfectly to the first 23 N-terminal amino acids of mature mouse anti-CEA gamma 1 chain as determined by amino acid sequence analysis of purified mouse anti-CEA gamma-1 chain. The coding region consists of 57 basepairs or 19 amino acids of presequences and 1346 basepairs or 447 amino acids of mature protein. The mature unglycosolated protein (MW 52,258) has a variable region of 135 amino acids, including a D region of 12 amino acids, and a J4 joining region of 13 amino acids. The constant region is 324 amino acids. After the stop codon behind amino acid 447 begins 96 bp of 3' untranslated sequences up to the polyA addition. The probe used to identify pγ298 and pγ11 hybridized to nucleotides 528–542 (FIG. **4**).

E.1.7 Construction of a Plasmid for Direct Expression of Mouse Mature Anti-CEA Kappa Chain Gene, pKCEAtrp207-1*

FIG. **6** illustrated the construction of pKCEAtrp207-1*

First, an intermediate plasmid pHGH207-1*, having a single trp promoter, was prepared as follows:

The plasmid pHGH 207 (described in U.S. patent application Ser. No. 307,473, filed Oct. 1, 1981 (EPO Publn. No. (0036776)) has a double lac promoter followed by the trp promoter, flanked by EcoR I sites and was used to prepare pHGH207-1. pHGH207 was digested with BamH 1, followed by partial digestion with EcoR I. The largest fragment, which contains the entire trp promoter, was isolated and ligated to the largest EcoR I- BamH I fragment from pBR322, and the ligation mixture used to transform *E. coli* 294. $Tet^R$ $Amp^R$ colonies were isolated, and most of them contained pHGH207-1. pHGH207-1* which lacks the EcoR1 site between the $amp^R$ gene and the trp promoter, was obtained by partial digestion of pHGH207-1 with EcoR I, filling in the ends with Klenow and dNTPs, and religation.

5 μg of pHGH207-1* was digested with EcoRI, and the ends extended to blunt ends using 12 units of DNA Polymerase I in a 50 μl reaction containing 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4) and 1 mM in each dNTP at 37° C. for 1 hour, followed by extraction with phenol/$CHCl_3$ and precipitation with ethanol. The precipitated DNA was digested with BamH I, and the large vector fragment (fragment 1) purified using 5 percent polyacrylamide gel electrophoresis, electroelution, phenol/$CHCl_3$ extraction and ethanol precipitation.

The DNA was resuspended in 50 μl of 10 mM Tris pH 8, 1 mM EDTA and treated with 500 units Bacterial Alkaline Phosphatase (BAP) for 30' at 65° followed by phenol/$CHCl_3$ extraction and ethanol precipitation.

A DNA fragment containing part of the light chain sequence was prepared as follows: 7 μg of pH17G4 DNA was digested with Pst I and the kappa chain containing cDNA insert was isolated by 6 percent gel electrophoresis, and electroelution. After phenol/$CHCl_3$ extraction, ethanol precipitation and resuspension in water, this fragment was digested with Ava II. The 333 bp Pst I-Ava II DNA fragment was isolated and purified from a 6 percent polyacrylamide gel.

A 15 nucleotide DNA primer was synthesized by the phosphotriester method G. O. 2,644,432 (supra) and has the following sequence:

```
Met Asp Ile Val Met
5' ATG GAC ATT GTT ATG 3'
```

The 5' methionine serves as the initiation codon. 500 ng of this primer was phosphorylated at the 5' end with 10 units T4 DNA kinase in 20 μl reaction containing 0.5 mM ATP. ~200 ng of the Pst I-Ava II DNA fragment was mixed with the 20 μl of the phosphorylated primer, heated to 95° C. for 3 minutes and quick frozen in a dry-ice ethanol bath. The denatured DNA solution was made 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4), 12 mM in each dNTP and 12 units DNA Polymerase I-Large Fragment was added. After 2 hours incubation at 37° C. this primer repair reaction was phenol/$CHCl_3$ extracted, ethanol precipitated, and digested to completion with Sau 3A. The reaction mixture was then electrophoresed on a 6 percent polyacrylamide gel and ~50 ng of the 182 basepair amino-terminal blunt-end to Sau 3A fragment (fragment 2) was obtained after electroelution.

100 ng of fragment 1 (supra) and 50 ng of fragment 2 were combined in 20 μl of 20 mM Tris HCl (pH 7.5), 10 mM $MgCl_2$, 10 mM DTT, 2.5 mM ATP and 1 unit of T4 DNA ligase. After overnight ligation at 14° C. the reaction was transformed into *E. coli* K12 strain 294. Restriction endonuclease digestion of plasmid DNA from a number of ampicillin resistant transformants indicated the proper construction and DNA sequence analysis proved the desired nucleotide sequence through the initiation codon of this new plasmid, pKCEAlnt1 (FIG. **6**).

The remainder of the coding sequence of the kappa light chain gene was prepared as follows:

The Pst I cDNA insert fragment from 7 μg of K17G4 DNA was partially digested with Ava II and the Ava II cohesive ends were extended to blunt ends in a DNA Polymerase I large fragment reaction. Following 6 percent polyacrylamide gel electrophoresis the 686 basepair Pst I to blunt ended Ava II DNA fragment was isolated, purified and subjected to Hpa II restriction endonuclease digestion. The 497 basepair Hpa II to blunt ended Ava II DNA fragment (fragment 3) was isolated and purified after gel electrophoresis.

10 μg of pKCEAlnt1 DNA was digested with Ava I, extended with DNA polymerase I large fragment, and

digested with Xba I. Both the large blunt ended Ava I to Xba I vector fragment and the small blunt ended Ava I to Xba I fragment were isolated and purified from a 6 percent polyacrylamide gel after electrophoresis. The large vector fragment (fragment 4) was treated with Bacterial Alkaline Phosphatase (BAP), and the small fragment was digested with Hpa II, electrophoresed on a 6 percent polyacrylamide and the 169 basepair Xba I-Hpa II DNA fragment (fragment 5) was purified. ~75 ng of fragment 4, ~50 ng of fragment 3 and ~50 ng of fragment 5 were combined in a T4 DNA ligase reaction and incubated overnight at 14°, and the reaction mixture transformed into *E. coli* K12 strain 294. Plasmid DNA from six ampicillin resistant transformants were analyzed by restriction endonuclease digestion. One plasmid DNA demonstrated the proper construction and was designated pKCEAInt2.

Final construction was effected by ligating the K-CEA fragment, including the trp promoter from pKCEAInt2 into pBR322(XAP). (pBR322(XAP) is prepared as described in U.S. application Ser. No. 452,227, filed Dec. 22, 1982; from pBR322 by deletion of the AvaI-PvuII fragment followed by ligation.)

The K-CEA fragment was prepared by treating pKCEAInt2 with Ava I, blunt ending with DNA polymerase I (Klenow fragment) in the presence of DNTPs, digestion with Pst I and isolation of the desired fragment by gel electrophoresis and electroelution.

The large vector fragment from pBR322(XAP) was prepared by successive treatment with EcoR I, blunt ending with polymerase, and redigestion with Pst I, followed by isolation of the large vector fragment by electrophoresis and electroelution.

The K-CEA and large vector fragments as prepared in the preceding paragraphs were ligated with T4 DNA ligase, and the ligation mixture transformed into *E. coli* as above. Plasmid DNA from several ampicillin resistant transformants were selected for analysis, and one plasmid DNA demonstrated the proper construction, and was designated pKCEAtrp207-1*.

E.1.8 Construction of a Plasmid Vector for Direct Expression of Mouse Mature Anti-CEA Heavy (Gamma 1) Chain Gene, pγCEAtrp207-1*

FIG. 7 illustrates the construction of pγCEAtrp207-1*. This plasmid was constructed in two parts beginning with construction of the C-terminal region of the gamma 1 gene.

5 μg of plasmid pHGH207-1* was digested with Ava I, extended to blunt ends with DNA polymerase I large fragment (Klenow fragment), extracted with phenol/$CHCl_3$, and ethanol precipitated. The DNA was digested with BamH I treated with BAP and the large fragment (fragment A) was purified by 6 percent polyacrylamide gel electrophoresis and electroelution.

~5 μg of pγ11 was digested with Pst I and the gamma chain cDNA insert fragment containing the C-terminal portion of the gene was purified, digested with Ava II followed by extension of the Ava II cohesive ends with Klenow, followed by Taq I digestion. The 375 basepair blunt ended Ava II to Taq I fragment (fragment B) was isolated and purified by gel electrophoresis and electroelution.

9 μg of pγ298 was digested with Taq I and BamH I for isolation of the 496 basepair fragment (fragment C).

Approximately equimolar amounts of fragments A, B, and C were ligated overnight at 14° in 20 μl reaction mixture, then transformed into *E. coli* strain 294. The plasmid DNA from six ampicillin resistant transformants was committed to restriction endonuclease analysis and one plasmid DNA, named pγCEAInt, demonstrated the correct construction of the C-terminal portion of gamma 1 (FIG. 5).

To obtain the N-terminal sequences, 30 μg of pγ298 was digested with Pst I and the 628 basepair DNA fragment encoding the N-terminal region of mouse anti-CEA gamma chain was isolated and purified. This fragment was further digested with Alu I and Rsa I for isolation of the 280 basepair fragment. A 15 nucleotide DNA primer

```
    met glu val met leu
5' ATG GAA GTG ATG CTG 3'
```

was synthesized by the phosphotriester method (supra).

The 5' methionine serves as the initiation codon. 500 ng of this synthetic oligomer primer was phosphorylated at the 5' end in a reaction with 10 units T4 DNA kinase containing 0.5 mM ATP in 20 μl reaction mixture. ~500 ng of the 280 basepair Alu I-Rsa I DNA fragment was mixed with the phosphorylated primer. The mixture was heat denatured for 3 minutes at 95° and quenched in dry-ice ethanol. The denatured DNA solution was made 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4), 12 mM in each dNTP and 12 units DNA Polymerase I-Large Fragment was added. After 2 hours incubation at 37° C., this primer repair reaction was phenol/$CHCl_3$ extracted, ethanol precipitated, and digested to completion with HpaII. ~50 ng of the expected 125 basepair blunt-end to Hpa II DNA fragment (fragment D) was purified from the gel.

A second aliquot of pγ298 DNA was digested with Pst I, the 628 basepair DNA fragment purified by polyacrylamide gel electrophoresis, and further digested with BamH I and Hpa II. The resulting 380 basepair fragment (fragment E) was purified by gel electrophoresis.

~5 μg of pγCEAIntI was digested with EcoR I, the cohesive ends were made flush with DNA polymerase I (Klenow), further digested with BamH I, treated with BAP and electrophoresed on a 6 percent polyacrylamide gel. The large vector fragment (fragment F) was isolated and purified.

In a three fragment ligation, 50 ng fragment D, 100 ng fragment E, and 100 ng fragment F were ligated overnight at 4° in a 20 μl reaction mixture and used to transform *E. coli* K12 strain 294. The plasmid DNAs from 12 ampicillin resistant transformants were analyzed for the correct construction and the nucleotide sequence surrounding the initiation codon was verified to be correct for the plasmid named pγCEAInt2.

The expression plasmid, pγCEAtrp207-1* used for expression of the heavy chain gene is prepared by a 3-way ligation using the large vector fragment from pBR322(XAP) (supra) and two fragments prepared from pγCEAInt2.

pBR322(XAP) was treated as above by digestion with EcoR1, blunt ending with DNA polymerase (Klenow) in the presence of dNTPs, followed by digestion with Pst I, and isolation of the large vector fragment by gel electrophoresis. A 1543 base pair fragment from pγCEAInt2 containing trp promoter linked with the N-terminal coding region of the heavy chain gene was isolated by treating pγCEAInt2 with Pst I followed by BamH I, and isolation of the desired fragment using PAGE. The 869 base pair fragment containing the C-terminal coding portion of the gene was prepared by partial digestion of pγCEAInt2 with Ava I, blunt ending with Klenow, and subsequent digestion with BamH I, followed by purification of the desired fragment by gel electrophoresis.

The aforementioned three fragments were then ligated under standard conditions using T4 DNA ligase, and a ligation mixture used to transform *E. coli* strain 294. Plasmid DNAs from several tetracycline resistant transformants were analyzed; one plasmid DNA demonstrated the proper construction and was designated pγCEAtrp207-1*.

E.1.9 Production of Immunoglobulin Chains by *E. coli*

*E. coli* strain W3110 (ATTC No. 27325) was transformed with pγCEAtrp207-1* or pKCEAtrp207-1* using standard techniques.

To obtain double transformants, *E. coli* strain W3110 cells were transformed with a modified pKCEAtrp207-1*, pKCEAtrp207-1*Δ, which had been modified by cleaving a Pst 1-Pvu I fragment from the amp$^R$ gene and religating. Cells transformed with pKCEAtrp207-1*Δ are thus sensitive to ampicillin but still resistant to tetracycline. Successful transformants were retransformed using pγCEAInt2 which confers resistance to ampicillin but not tetracycline. Cells containing both pKCEAtrp207-1*Δ and pγCEAInt2 thus identified by growth in a medium containing both ampicillin and tetracycline.

To confirm the production of heavy and/or light chains in the transformed cells, the cell samples were inoculated into M9 tryptophan free medium containing 10 μg/ml tetracycline, and induced with indoleacrylic acid (IAA) when the OD 550 reads 0.5. The induced cells were grown at 37° C. during various time periods and then spun down, and suspended in TE buffer containing 2 percent SDS and 0.1 M β-mercaptoethanol and boiled for 5 minutes. A 10xvolume of acetone was added and the cells kept at 22° C. for 10 minutes, then centrifuged at 12,000 rpm. The precipitate was suspended in O'Farrell SDS sample buffer (O'Farrell, P. H., *J. Biol. Chem.*, 250: 4007 (1975)); boiled 3 minutes, recentrifuged, and fractionated using SDS PAGE (10 percent), and stained with silver stain (Goldman, D. et al., *Science* 211: 1437 (1981)); or subjected to Western blot using rabbit anti-mouse IgG (Burnett, W. N., et al., *Anal. Biochem.* 112: 195 (1981)), for identification light chain and heavy chain.

Cells transformed with pγCEAtrp207-1* showed bands upon SDS PAGE corresponding to heavy chain molecular weight as developed by silver stain. Cells transformed with pKCEAtrp207-1* showed the proper molecular weight band for light chain as identified by Western blot; double transformed cells showed bands for both heavy and light chain molecular weight proteins when developed using rabbit anti-mouse IgG by Western blot. These results are shown in FIGS. **8A**, **8B**, and **8C**.

FIG. **8A** shows results developed by silver stain from cells transformed with pγCEAtrp207-1*. Lane 1 is monoclonal anti-CEA heavy chain (standard) from CEA.66-E3. Lanes 2b–5b are timed samples 2 hrs, 4 hrs, 6 hrs, and 24 hrs after IAA addition. Lanes 2a–5a are corresponding untransformed controls; Lanes 2c–5c are corresponding uninduced transformants.

FIG. **8B** shows results developed by Western blot from cells transformed with pKCEAtrp207-1*. Lanes 1b–6b are extracts from induced cell immediately, 1 hr, 3.5 hrs, 5 hrs, 8 hrs, and 24 hrs after IAA addition, and 1a–6a corresponding uninduced controls. Lane 7 is an extract from a pγCEAtrp207-1* control, lanes 8, 9, and 10 are varying amounts of anti CEA-kappa chain from CEA.66-E3 cells.

FIG. **8C** shows results developed by Western blot from four colonies of double transformed cells 24 hours after IAA addition (lanes 4–7). Lanes 1–3 are varying amounts of monoclonal gamma chain controls, lanes 8 and 9 are untransformed and pγCEAtrp207-1* transformed cell extracts, respectively.

In another quantitative assay, frozen, transformed *E. coli* cells grown according to E.1.10 (below) were lysed by heating in sodium dodecyl sulfate (SDS) β-mercaptoethanol cell lysis buffer at 100°. Aliquots were loaded on an SDS polyacrylamide gel next to lanes loaded with various amounts of hybridoma anti-CEA. The gel was developed by the Western blot, Burnett (supra), using $^{125}$I-labeled sheep anti-mouse IgG antibody from New England Nuclear. The results are shown in FIG. **9**. The figure shows that the *E. coli* products co-migrate with the authentic hybridoma chains, indicating no detectable proteolytic degradation in *E. coli*. Heavy chain from mammalian cells is expected to be slightly heavier than *E. coli* material due to glycosylation in the former. Using the hybridoma lanes as a standard, the following estimates of heavy and light chain production were made:

| | (Per gram of cells) |
|---|---|
| *E. coli* (W3110/pγCEAtrp207-1*) | 5 mg γ |
| *E. coli* (W3110/pKCEAtrp207-1*) | 1.5 mg K |
| *E. coli* (W3110/pKCEAtrp207-1*Δ, pγCEAInt2) | 0.5 mg K, 1.0 mg γ |

E.1.10 Reconstitution of Antibody from Recombinant K and Gamma Chains

In order to obtain heavy and light chain preparations for reconstitution, transformed cells were grown in larger batches, harvested and frozen. Conditions of growth of the variously transformed cells were as follows:

*E. coli* (W3110/pγCEAtrp207-1*) were inoculated into 500 ml LB medium containing 5 μg/ml tetracycline and grown on a rotary shaker for 8 hours. The culture was then transferred to 10 liters of fermentation medium containing yeast nutrients, salts, glucose, and 2 μg/ml tetracycline. Additional glucose was added during growth and at OD 550=20, indoleacrylic (IAA), a trp derepressor, was added to a concentration of 50 μg/ml. The cells were fed additional glucose to a final OD 550=40, achieved approximately 6 hours from the IAA addition.

*E. coli* (W3110) cells transformed with pKCEA trp 207-1* and double transformed (with pKCEAtrp207-1*Δ and pγCEAInt2) were grown in a manner analogous to that described above except that the OD 550 six hours after IAA addition at harvest was 25–30.

The cells were then harvested by centrifugation, and frozen.

E.2 Assay Method for Reconstituted Antibody

Anti-CEA activity was determined by ELISA as a criterion for successful reconstitution. Wells of microtiter plates (Dynatech Immulon) were saturated with CEA by incubating 100 μl of 2–5 μg CEA/ml solution in 0.1M carbonate buffer, pH 9.3 for 12 hours at room temperature. The wells were then washed 4 times with phosphate buffered saline (PBS), and then saturated with BSA by incubating 200 μl of 0.5 percent BSA in PBS for 2 hours at 37° C., followed by washing 4 times with PBS. Fifty microliters of each sample was applied to each well. A standard curve (shown in FIG. **10**), was run, which consisted of 50 μl samples of 10 μg, 5 μg, 1 μg, 500 ng, 100 ng, 50 ng, 10 ng, 5 ng and 1 ng anti-CEA/ml in 0.5 percent BSA in PBS, plus 50 μl of 0.5 percent BSA in PBS alone as a blank. All of the samples were incubated in the plate for 90 minutes at 37° C.

The plates were then washed 4 times with PBS, and sheep anti-mouse IgG-alkaline phosphate (TAGO, Inc.) was applied to each well by adding 100 μl of an enzyme concentration of 24 units/ml in 0.5 percent BSA in PBS. The solution was incubated at 37° C. for 90 minutes. The plates were washed 4 times with PBS before adding the substrate, 100 μl of a 0.4 mg/ml solution of p-nitrophenylphosphate (Sigma) in ethanolamine buffered saline, pH 9.5. The substrate was incubated 90 minutes at 37° C. for color development.

The $A_{450}$ of each well was read by the Microelisa Auto Reader (Dynatech) set to a threshold of 1.5, calibration of 1.0 and the 0.5 percent BSA in PBS (Blank) well set to 0.000. The $A_{450}$ data was tabulated in RS-1 on the VAX system, and the standard curve data fitted to a four-parameter logistic model. The unknown samples' concentration were calculated based on the $A_{450}$ data.

E.3 Reconstitution of Recombinant Antibody and Assay

Frozen cells prepared as described in paragraph E.1.10 were thawed in cold lysis buffer [10 mM Tris HCl, pH 7.5, 1 mM EDTA, 0.1M NaCl, 1 mM phenylmethylsulfonyl fluoride (PMSF)] and lysed by sonication. The lysate was partially clarified by centrifugation for 20 mins at 30,000 rpm. The supernatant was protected from proteolytic enzymes by an additional 1 mM PMSF, and used immediately or stored frozen at –80° C.; frozen lysates were never thawed more than once.

The S-sulfonate of *E. coli* produced anti-CEA heavy chain (γ) was prepared as follows: Recombinant *E. coli* cells transformed with pγCEAtrp207-1* which contained heavy chain as insoluble bodies, were lysed and centrifuged as above; the pellet was resuspended in the same buffer, sonicated and re-centrifuged. This pellet was washed once with buffer, then suspended in 6M guanidine HCl, 0.1M Tris HCl, pH 8, 1 mM EDTA, 20 mg/ml sodium sulfite and 10 mg/ml sodium tetrathionate and allowed to react at 25° for about 16 hrs. The reaction mixture was dialyzed against 8M urea, 0.1M Tris HCl, pH 8, and stored at 4°, to give a 3 mg/ml solution of γ-$SSO_3$.

650 μl of cell lysate from cells of various *E. coli* strains producing various IgG chains, was added to 500 mg urea. To this was added β-mercaptoethanol to 20 mM, Tris-HCl, pH 8.5 to 50 mM and EDTA to 1 mM, and in some experiments, γ-$SSO_3$ was added to 0.1 mg/ml. After standing at 25° for 30–90 mins., the reaction mixtures were dialyzed at 4° against a buffer composed of 0.1M sodium glycinate, pH 10.8, 0.5M urea, 10 mM glycine ethyl ester, 5 mM reduced glutathione, 0.1 mM oxidized glutathione. This buffer was prepared from $N_2$-saturated water and the dialysis was performed in a capped Wheaton bottle. After 16–48 hours, dialysis bags were transferred to 4° phosphate buffered saline containing 1 mM PMSF and dialysis continued another 16–24 hrs. Dialysates were assayed by ELISA as described in paragraph E.2 for ability to bind CEA. The results below show the values obtained by comparison with the standard curve in x ng/ml anti-CEA. Also shown are the reconstitution efficiencies calculated from the ELISA responses, minus the background (108 ng/ml) of cells producing K chain only, and from estimates of the levels of γ and K chains in the reaction mixtures.

| | ng/ml anti-CEA | Percent recombination |
|---|---|---|
| *E. coli* W3110 producing IFN-αA (control) | 0 | — |
| *E. coli* (W3110/pKCEAtrp207-1*) | 108 | — |
| *E. coli* (W3110/pKCEAtrp207-1*), plus γ-$SSO_3$ | 848 | 0.33 |
| *E. coli* (W3110/pKCEAtrp207-1*Δ, pγCEAInt2) | 1580 | 0.76 |
| Hybridoma anti-CEA K-$SSO_3$ and γ-$SSO_3$ | 540 | 0.40 |

E.4 Preparation of Chimeric Antibody

FIGS. **11** and **12** show the construction of an expression vector for a chimeric heavy (gamma) chain which comprises the murine anti CEA variable region and human γ-2 constant region.

A DNA sequence encoding the human gamma-2 heavy chain is prepared as follows: the cDNA library obtained by standard techniques from a human multiple myeloma cell line is probed with 5' GGGCACTCGACACAA 3' to obtain the plasmid containing the cDNA insert for human gamma-2 chain (Takahashi, et al., *Cell*, 29: 671 (1982), incorporated herein by reference), and analyzed to verify its identity with the known sequence in human gamma-2 (Ellison, J., et al., *Proc. Natl. Acad. Sci. (USA)*, 79: 1984 (1982) incorporated herein by reference).

As shown in FIG. **11**, two fragments are obtained from this cloned human gamma 2 plasmid (pγ2). The first fragment is formed by digestion with PvuII followed by digestion with Ava III, and purification of the smaller DNA fragment, which contains a portion of the constant region, using 6 percent PAGE. The second fragment is obtained by digesting the pγ2 with any restriction enzyme which cleaves in the 3' untranslated region of γ2, as deduced from the nucleotide sequence, filling in the Klenow and dNTPs, cleaving with Ava III, and isolating the smaller fragment using 6 percent PAGE. (The choice of a two step, two fragment composition to supply the PvuII-3' untranslated fragment provides a cleaner path to product due to the proximity of the AvaIII site to the 3 terminal end thus avoiding additional restriction sites in the gene sequence matching the 3' untranslated region site.) pγCEA207-1* is digested with EcoR 1, treated with Klenow and dNTPs to fill in the cohesive end, and digested with Pvu II, the large vector fragment containing promoter isolated by 6 percent PAGE.

The location and DNA sequence surrounding the PvuII site in the mouse gamma-1 gene are identical to the location and DNA sequence surrounding the PvuII site in the human gamma-2 gene.

The plasmid resulting from a three way ligation of the foregoing fragments, pChim1, contains, under the influence of trp promoter, the variable and part of the constant region of murine anti-CEA gamma 1 chain, and a portion of the gamma 2 human chain. pChim1 will, in fact, express a chimeric heavy chain when transformed into *E. coli*, but one wherein the change from mouse to human does not take place at the variable to constant junction.

FIG. **12** shows modification of pChim1 to construct pChim2 so that the resulting protein from expression will contain variable region from murine anti CEA antibody and constant region from the human γ-2 chain. First, a fragment is prepared from pChim1 by treating with Nco I, blunt ending with Klenow and dNTPs, cleaving with Pvu II, and isolating the large vector fragment which is almost the complete plasmid except for short segment in the constant coding region for mouse anti CEA. A second fragment is prepared from the previously described pγ2 by treating with Pvu II, followed by treating with any restriction enzyme which cleaves in the variable region, blunt ending with Klenow and dNTPs and isolating the short fragment which comprises the junction between variable and constant regions of this chain.

Ligation of the foregoing two fragments produces an intermediate plasmid which is correct except for an extraneous DNA fragment which contains a small portion of the constant region of the murine anti CEA antigen, and a small portion of the variable region of the human gamma chain. This repair can be made by excising the Xba I to Pvu II fragment and cloning into M13 phage as described by Messing et al., *Nucleic Acids Res.* 9: 309 (1981), followed by in vitro site directed deletion mutagenesis as described by Adelman, et al., *DNA*, in press (1983) which is incorporated

herein by reference. The Xba I-Pvu II fragment thus modified is ligated back into the intermediate plasmid to form pChim2. This plasmid then is capable of expressing in a suitable host a cleanly constructed murine variable/human constant chimeric heavy chain.

In an analogous fashion, but using mRNA templates for cDNA construction for human kappa rather than γ chain, the expression plasmid for chimeric light chain is prepared.

The foregoing two plasmids are then double transformed into *E. coli* W3110, the cells grown and the chains reconstituted as set forth in paragraph E.1–E.3 supra.

E.5 Preparation of Altered Murine Anti-CEA Antibody

E.5.1 Construction of Plasmid Vectors for Direct Expression of Altered Murine Anti-CEA Heavy Chain Gene

The cysteine residues, and the resultant disulfide bonds in the region of amino acids 216–230 in the constant region of murine anti-CEA heavy chain are suspected to be important for complement fixation (Klein, et al., *Proc. Natl. Acad. Sci., (USA)*, 78: 524 (1981)) but not for the antigen binding property of the resulting antibody. To decrease the probability of incorrect disulfide bond formation during reconstitution according to the process of the invention herein, the nucleotides encoding the amino acid residues 226–232 which includes codons for three cysteines, are deleted as follows:

A "deleter" deoxyoligonucelotide, 5' CTAACACCATGTCAGGGT is used to delete the relevant portions of the gene from pγCEAtrp207-1* by the procedure of Wallace, et al., *Science*, 209: 1396 (1980) or of Adelman, et al., *DNA* 2, 183 (1983). Briefly, the "deleter" deoxyoligonucelotide is annealed with denatured pγCEAtrp207-1* DNA, and primer repair synthesis carried out in vitro, followed by screening by hybridization of presumptive deletion clones with $P^{32}$ labelled deleter sequence.

E.5.2 Production of Cysteine Deficient Altered Antibody

The plasmid prepared in E.5.1 is transformed into an *E. coli* strain previously transformed with pKCEAtrp207-1* as described above. The cells are grown, extracted for recombinant antibody chains, and the altered antibody reconstituted as described in E.1.10.

E.6 Preparation of Fab

E.6.1 Construction of a Plasmid Vector for Direct Expression of Murine Anti-CEA Gamma 1 Fab Fragment Gene pγCEAFabtrp207-1*

FIG. **13** presents the construction of pγCEAFabtrp207-1*. 5 μg of pBR322 was digested with Hind III, the cohesive ends made flush by treating with Klenow and dNTPs; digested with Pst I, and treated with BAP. The large vector fragment, fragment **I**, was recovered using 6 percent PAGE followed by electroelution.

5 μg of pγCEAtrp207-1* was digested with both BamH I and Pst I and the ~1570 bp DNA fragment (fragment II) containing the trp promoter and the gene sequence encoding the variable region continuing into constant region and further into the anti-CEA gamma 1 chain hinge region, was isolated and purified after electrophoresis.

Expression of the anti-CEA gamma 1 chain Fab fragment rather than complete heavy chain requires that a termination codon be constructed at the appropriate location in the gene. For this, the 260 bp Nco I-Nde I DNA fragment from 20 μg of the pγ298 was isolated and purified. A 13 nucleotide DNA primer, the complement of which encodes the last 3 C-terminal amino acids of the Fab gene and 2 bases of the 3 needed for the stop codon, was synthesized by the phosphotriester method (supra). The probe hybridizes to nucleotides 754 to 767 (FIG. **4**) which has the following sequence:

```
AspCysGlyStop
5' GGGATTGTGGTTG  3'
```

The third base of the stop codon is provided by the terminal nucleotide of the filled-in Hind III site from pBR322 cleavage described above. 500 ng of this primer was used in a primer repair reaction by phosphorylation at the 5' end in a reaction with 10 units T4 DNA kinase containing 0.5 mM ATP in 20 μl, and mixing with ~200 ng of the Nco I-Nde I DNA fragment. The mixture was heat denatured for 3 minutes at 95° and quenched in dry-ice ethanol. The denatured DNA solution was made 60 mM NaCl, 7 mM $MgCl_2$, 7 mM Tris HCl (pH 7.4), 12 mM in each dNTP and 12 units DNA Polymerase I-Large Fragment was added. After 2 hours incubation at 37° C., this primer repair reaction was phenol/$CHCl_3$ extracted, ethanol precipitated, digested with BamH I and the reaction electrophoresed through a 6 percent polyacrylamide gel. ~50 ng of the 181 bp blunt end to BamH I DNA fragment, fragment III, was isolated and purified.

~100 ng of fragment I, ~100 ng each of fragments II and III were ligated overnight and transformed into *E. coli* K12 strain 294. Plasmid DNA from several tetracycline resistant transformants was analyzed for the proper construction and the nucleotide sequence through the repair blunt end filled-in Hind III junction was determined for verification of the TGA stop codon.

E.6.2 Production of Fab Protein

The plasmid prepared in E.6.1 is transformed into an *E. coli* strain previously transformed with pKCEAtrp207-1* as described above. The cells are grown, extracted for recombinant antibody chains and the Fab protein reconstituted as described in E.1.10.

What is claimed is:

**1**. A process for producing an immunoglobulin molecule or an immunologically functional immunoglobulin fragment comprising at least the variable domains of the immunoglobulin heavy and light chains, in a single host cell, comprising the steps of:

(i) transforming said single host cell with a first DNA sequence encoding at least the variable domain of the immunoglobulin heavy chain and a second DNA sequence encoding at least the variable domain of the immunoglobulin light chain, and

(ii) independently expressing said first DNA sequence and said second DNA sequence so that said immunoglobulin heavy and light chains are produced as separate molecules in said transformed single host cell.

**2**. The process according to claim **1** wherein said first and second DNA sequences are present in different vectors.

**3**. The process according to claim **1** wherein said first and second DNA sequences are present in a single vector.

**4**. A process according to claim **3** wherein the vector is a plasmid.

**5**. The process according to claim **4** wherein the plasmid is pBR322.

**6**. The process according to claim **1** wherein the host cell is a bacterium or yeast.

**7**. The process according to claim **6** wherein the host cell is *E. coli* or *S. cerevisiae*.

**8**. A process according to claim **7** wherein the host cell is *E. coli* strain X1776 (ATCC No. 31537).

**9**. A process according to claim **1** wherein the immunoglobulin heavy and light chains are expressed in the host cell and secreted therefrom as an immunologically functional immunoglobulin molecule or immunoglobulin fragment.

10. A process according to claim 1 wherein the immunoglobulin heavy and light chains are produced in insoluble form and are solubilized and allowed to refold in solution to form an immunologically functional immunoglobulin molecule or immunoglobulin fragment.

11. A process according to claim 1 wherein the DNA sequences code for the complete immunoglobulin heavy and light chains.

12. The process according to claim 1 wherein said first or said second DNA sequence further encodes at least one constant domain, wherein the constant domain is derived from the same source as the variable domain to which it is attached.

13. The process according to claim 1 wherein said first or said second DNA sequence further encodes at least one constant domain, wherein the constant domain is derived from a species or class different from that from which the variable domain to which it is attached is derived.

14. The process according to claim 1 wherein said first and second DNA sequences are derived from one or more monoclonal antibody producing hybridomas.

15. A vector comprising a first DNA sequence encoding at least a variable domain of an immunoglobulin heavy chain and a second DNA sequence encoding at least a variable domain of an immunoglobulin light chain wherein said first DNA sequence and said second DNA sequence are located in said vector at different insertion sites.

16. A vector according to claim 15 which is a plasmid.

17. A host cell transformed with a vector according to claim 15.

18. A transformed host cell comprising at least two vectors, at least one of said vectors comprising a DNA sequence encoding at least a variable domain of an immunoglobulin heavy chain and at least another one of said vectors comprising a DNA sequence encoding at least the variable domain of an immunoglobulin light chain.

19. The process of claim 1 wherein the host cell is a mammalian cell.

20. The transformed host cell of claim 18 wherein the host cell is a mammalian cell.

21. A method comprising

a) preparing a DNA sequence consisting essentially of DNA encoding an immunoglobulin consisting of an immunoglobulin heavy chain and light chain or Fab region, said immunoglobulin having specificity for a particular known antigen;

b) inserting the DNA sequence of step a) into a replicable expression vector operably linked to a suitable promoter;

c) transforming a prokaryotic or eukaryotic microbial host cell culture with the vector of step b);

d) culturing the host cell; and

e) recovering the immunoglobulin from the host cell culture, said immunoglobulin being capable of binding to a known antigen.

22. The method of claim 21 wherein the heavy and light chain are the heavy and light chains of anti-CEA antibody.

23. The method of claim 21 wherein the heavy chain is of the gamma family.

24. The method of claim 21 wherein the light chain is of the kappa family.

25. The method of claim 21 wherein the vector contains DNA encoding both a heavy chain and a light chain.

26. The method of claim 21 wherein the host cell is *E. coli* or yeast.

27. The method of claim 26 wherein the heavy chain and light chains or Fab region are deposited within the cells as insoluble particles.

28. The method of claim 27 wherein the heavy and light chains are recovered from the particles by cell lysis followed by solubilization in denaturant.

29. The method of claim 21 wherein the heavy and light chains are secreted into the medium.

30. The method of claim 21 wherein the host cell is a gram negative bacterium and the heavy and light chains are secreted into the periplasmic space of the host cell bacterium.

31. The method of claim 21 further comprising recovering both heavy and light chain and reconstituting light chain and heavy chain to form an immunoglobulin having specific affinity for a particular known antigen.

32. The insoluble particles of heavy chain and light chains or Fab region produced by the method of claim 27.

33. A process for producing an immunoglobulin molecule or an immunologically functional immunoglobulin fragment comprising at least the variable domains of the immunoglobulin heavy and light chains, in a single host cell, comprising:

independently expressing a first DNA sequence encoding at least the variable domain of the immunoglobulin heavy chain and a second DNA sequence encoding at least the variable domain of the immunoglobulin light chain so that said immunoglobulin heavy and light chains are produced as separate molecules in said single host cell transformed with said first and second DNA sequences.

34. The process of claim 9, further comprising the step of attaching the immunoglobulin molecule or immunoglobulin fragment to a label or drug.

35. The process of claim 10, further comprising the step of attaching the immunoglobulin molecule or immunoglobulin fragment to a label or drug.

36. The process of claim 33, further comprising the step of attaching the immunoglobulin molecule or immunoglobulin fragment to a label or drug.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

# CERTIFICATE OF CORRECTION

PATENT NO. : 6,331,415 B1
DATED : December 18, 2001
INVENTOR(S) : Shmuel Cabilly et al.



It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page,
Item [73], Assignee, please insert -- City of Hope, Duarte, CA (US) --.

Column 19,
Line 56, please change "BamH 1" to -- BamH I --.

Signed and Sealed this

Twenty-fifth Day of June, 2002

*Attest:*

*Attesting Officer*

JAMES E. ROGAN
*Director of the United States Patent and Trademark Office*

(5)

SUPREME COURT, U.S.
FILED
MAY 2006
OFFICE OF THE CLERK

No. 05-608

IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner*,

v.

GENENTECH, INC., *et al.*,

*Respondents*.

**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

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## QUESTION PRESENTED

Does Article III's grant of jurisdiction of "all Cases . . . arising under . . . the Laws of the United States," implemented in the "actual controversy" requirement of the Declaratory Judgment Act, 28 U.S.C. § 2201(a), require a patent licensee to refuse to pay royalties and commit material breach of the license agreement before suing to declare the patent invalid, unenforceable or not infringed?

## LIST OF PARTIES

Petitioner was the only appellant in the court below. Appellees in that Court were Genentech, Inc., City of Hope National Medical Center, and Celltech R & D, Ltd.

## LIST PURSUANT TO RULE 29.6

Petitioner is a publicly held corporation. No publicly held entity owns 10% or more of its stock.

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IN THE

# Supreme Court of the United States

NO. 05-608

MEDIMMUNE, INC.,

*Petitioner*,

v.

GENENTECH, INC., *et al.*,

*Respondents*.

**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## BRIEF FOR PETITIONER

## OPINIONS BELOW

The opinion of the United States District Court for the Central District of California is unreported and is reproduced at P.C.A. 21a.[1] The opinion of the United States Court of Appeals for the Federal Circuit is reported at 427 F.3d 958 and is reproduced at P.C.A. 1a.

## JURISDICTION

The judgment of the Court of Appeals was entered October 18, 2005. P.C.A. 1a, J.A. 455. The petition for certiorari was filed November 10, 2005, and granted February 21, 2006.

[1] Citations to "P.C.A." are to the appendix to the petition for certiorari. Citations to "J.A." are to the joint appendix.

J.A. 458. This Court has jurisdiction pursuant to 28 U.S.C. § 1254(1).

## CONSTITUTIONAL AND STATUTORY PROVISIONS AND RULE INVOLVED

Article III, § 2, of the Constitution of the United States, and relevant portions of 28 U.S.C. §§ 1331, 1338, 2201 and 2202, 35 U.S.C. §§ 135, 282, 283, 284 and 285, and Rule 57, Fed. R. Civ. P., are reproduced in the addendum.

## STATEMENT

Petitioner, MedImmune, Inc., is a biotechnology company in Gaithersburg, Maryland, founded in 1988. Unlike traditional pharmaceutical manufacturers, which develop and market chemical compounds, MedImmune uses "bioengineering" to alter the genetic arrangement of living cells so that they produce antibodies (immunoglobulins) for use as medications targeted specifically at particular harmful viruses and agents that can attack the human body.

### A. MedImmune's Development of Synagis®.

After seven years of effort and expense for research, development and many clinical trials, MedImmune in 1998 received approval from the U.S. Food and Drug Administration for Synagis® (palivizumab), a bioengineered antibody that prevents infection from RSV (respiratory syncytial virus), a contagious viral condition dangerous to vulnerable infants. Nearly all young children contract RSV, half of them in the first year of life, and soon recover. But RSV infections are a serious threat to high-risk pediatric patients—particularly to newborns with low birth weight, whose natural immune systems are not sufficiently developed to recognize and combat RSV, and also to children with chronic heart or lung ailments. For such vulnerable infants, RSV infection unless prevented can be fatal.

To develop Synagis®, MedImmune's scientists using recombinant DNA technology reengineered mouse genes that

encoded an RSV antibody in mice, removed most mouse-specific features, and replaced those with human ones. Synagis® is classified as a "humanized monoclonal antibody," *i.e.*, an animal antibody modified into a predominantly human one ("humanized"), and produced as identical copies from a single type of cell ("monoclonal"). When introduced into the human body, Synagis® neutralizes the RSV virus before infection can occur. Synagis® was the first monoclonal antibody successfully developed to combat an infectious disease. In 1998 MedImmune was granted U.S. Patent No. 5,824,307 for the Synagis® antibody and methods of using it. Hospitalization of children for RSV infection has dropped sharply since the introduction of Synagis®.[2]

**B. The 1997 License.**

Respondent Genentech, Inc., owns U.S. Patent No. 4,816,567 ("the Cabilly I patent"), applied for April 8, 1983, and issued March 28, 1989, to inventors Shmuel Cabilly, *et al.* J.A. 485. The Cabilly I patent was directed to a process for synthesizing monoclonal antibodies that are "chimeric," *i.e.*, containing a relatively high proportion of animal to human components. On June 4, 1997, a year prior to the FDA approval of Synagis®, MedImmune accepted a license from Genentech covering any anti-RSV monoclonal antibody MedImmune might thereafter make, use or sell that would be covered by the Cabilly I "chimeric" patent, J.A. 399, or by "continuations" of the Cabilly I patent, including a pending "coexpression" patent application, the exact claims of which were not disclosed. *Id.* At the time of the license it was

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[2] See National Institutes of Health Office of Technology Transfer, *Synagis® Helping Infants and Parents Breathe Easier: A Case Study* 2 (2002); Meissner *et al.*, *Revised Indications for the Use of Palivizumab and RSV Immune Globulin Intravenous for the Prevention of RSV Infections*, 112 PEDIATRICS 1447 (2003). Synagis® currently is administered annually to approximately 180,000 infants in the United States, and is widely used in other countries.

uncertain whether that pending application ever would be granted, and if it were to be, what would be the scope of its claims. The license called for an initial licensing fee and subsequent quarterly royalties based on revenues from "Licensed Product(s)," defined as those that "would, if not licensed under this Agreement, infringe one or more claims of either or both" of the patents included. J.A. 399, 402-03. The license contained no mention of Synagis®. The license contemplated that the licensed patents and applications might not be valid, and that MedImmune's products might not infringe, in which event no royalty would be due. J.A. 399; see also J.A. 411. The license contained no promise by MedImmune not to sue or to challenge patent validity.

When Synagis® became available in September 1998, MedImmune concluded that respondents' Cabilly I patent—which dealt with chimeric, rather than humanized, antibodies—did not cover Synagis®, so that Synagis® was not a "Licensed Product" under the 1997 license. J.A. 399, 416. Accordingly, MedImmune never paid any royalties to Genentech under the 1997 license of the Cabilly I patent for sales of Synagis®. J.A. 388, 416. The Cabilly I patent expired March 28, 2006.

### C. Genentech's 2001 Cabilly II Patent.

Genentech's patent application referred to in the 1997 license agreement, J.A. 399, had been filed in 1988 and shortly thereafter became the subject of a prolonged dispute between Genentech and a British firm, Celltech R&D, Ltd., concerning which firm's scientists were the first inventors. In 1989, Celltech had obtained U.S. Patent No. 4,816,397, naming Michael A. Boss as the first inventor ("the Boss patent"). J.A. 459. Shortly thereafter Genentech amended its pending patent application to add eighteen much broader claims that concededly had been copied essentially verbatim from the Boss patent. *Compare* J.A. 484 *with* J.A. 549-50. These claims purported to cover the process of producing

any type of monoclonal antibody—chimeric, humanized, or other—in one cell using recombinant DNA techniques. Genentech's amendment expectably triggered a contested patent-interference proceeding against Celltech in the U.S. Patent and Trademark Office (PTO), in which Genentech contended that Cabilly, not Boss, was the first inventor, and that its application was entitled to priority over Celltech's Boss Patent.

After seven years of administrative litigation, the PTO in 1998 confirmed that Celltech, not Genentech, was entitled to its patent based on priority of invention. *Cabilly* v. *Boss*, 55 U.S.P.Q.2d 1238 (PTO Bd. Pat. App. & Int. 1998). But in 2001, after Genentech sought judicial review pursuant to 35 U.S.C. § 146, J.A. 276, the two companies settled. J.A. 334. In stipulated findings and judgment drafted by the parties' attorneys, Celltech agreed—disavowing its own victory in the PTO decision—that Genentech had priority of invention, that Celltech's Boss patent (nearing its 2006 expiration date) should be cancelled, and that a new patent based on the broad claims and with an expiration seventeen years in the future should issue to Genentech. J.A. 334, 343-46, 347-48. In return Celltech received money payments and valuable "preferential" rights under the new patent. J.A. 106-08, 228; Ct. Apps. J.A. 1697, 1713. The PTO on remand from the court declared the claims of Celltech's Boss patent void, based on the stipulated court judgment, but commenting on the irregular judicial procedure observed that the effect of that judgment was to grant Genentech a patent with a term of 29 years:

> "We will note that if a patent is issued to Cabilly, its term will begin to run now and the public has already been subject to patent rights of Boss since 1989, and that the interference has been pending since 1991."

*Cabilly* v. *Boss*, 60 U.S.P.Q.2d 1752, 1755 n.7 (P.T.O. Bd. Pat. App. & Int. 2001). Nevertheless, on December 18, 2001,

the PTO issued to Genentech U.S. Patent 6,331,415 B1 ("the Cabilly II patent"), with a term lasting until 2018. J.A. 509.

Upon that issuance in 2001—four years after the 1997 license agreement—the exact scope of the claims of the Cabilly II patent was publicly disclosed for the first time. Genentech in a press release described its new patent as a "Fundamental U.S. Patent for Antibody Technology" that "covers a principal way that therapeutic and diagnostic antibodies are made by biotechnology and pharmaceutical companies and others using recombinant DNA technology." J.A. 417. The biotechnology press called it "a patent claiming broad rights to fundamental methods for the recombinant expression of antibodies" that "could potentially block the production of antibody products by rival companies or increase their royalty burden." J.A. 423.

### D. Genentech's Infringement Charge and Demand for Royalties.

Within days of issuance of the Cabilly II patent on December 18, 2001, a member of Genentech's legal staff telephoned a senior officer at MedImmune to announce that Synagis®, on the market since 1998, infringed the new Cabilly II patent, and that therefore it was a "Licensed Product" for which royalties must be paid under the 1997 license. J.A. 419. By letter of January 7, 2002, Genentech followed up with a written notice

> "to confirm Genentech's expectation that MedImmune will pay royalties on sales of its Synagis® antibody product pursuant to the license granted by Genentech under the recently issued U.S. Patent No. 6,331,415."

*Id.* MedImmune in response asked to know Genentech's "basis for believing that MedImmune's product would infringe any valid claim of the '415 [Cabilly II] Patent such that royalties would be due." J.A. 421. Receiving no re-

sponse for several weeks, MedImmune explained that it had wired a payment:

> "Such payment, however, was made under protest and with reservation of all of our rights."

J.A. 426. MedImmune also warned that it would "evaluate how further to proceed." *Id.* Genentech reiterated its infringement claim. J.A. 428.

Based on the communications from Genentech asserting that Synagis® infringed the Cabilly II patent and demanding royalties, and also on Genentech's "public statements about the breadth and importance of the Cabilly II patent," J.A. 388; see J.A. 417, MedImmune concluded "that Genentech would terminate the 1997 License Agreement and sue MedImmune for patent infringement based on sales of Synagis® if MedImmune did not make the royalty payments as demanded," J.A. 388. MedImmune "chose not to risk . . . the potential imposition of a preliminary or permanent injunction that would prevent MedImmune from selling the product." J.A. 389. "Accordingly, MedImmune decided to pay royalties under protest . . . and subsequently challenge in court whether the Cabilly II patent was valid, enforceable and/or infringed by MedImmune's Synagis® product." *Id.* The dispute remained unresolved while MedImmune continued to pay the sums demanded for Synagis®, and continued to do business with Genentech on other products. *E.g.*, J.A. 437.

### E. The District Court Proceeding.

With demand for Synagis® growing, and payments to Genentech correspondingly rising, on April 11, 2003, MedImmune brought suit in the United States District Court for the Central District of California under, *inter alia*, 28 U.S.C. §§ 1331 and 1338. J.A. 41, 103. The complaint sought a declaratory judgment under 28 U.S.C. § 2201(a) against respondents Genentech and City of Hope, a co-owner, that the Cabilly II patent was invalid as anticipated, obvious, not adequately described and not enabled (35 U.S.C. §§ 101, 102,

103, 112), J.A. 136-37; unenforceable because Genentech had knowingly failed to disclose material prior art and in other respects misled the Patent and Trademark Office, J.A. 106-30, 137-40; and not infringed by Synagis®, so that royalties were not due under the license. P.C.A. 29a; J.A. 43, 46, 60-63, 105, 136-41, 147.

Neither respondent questioned the District Court's jurisdiction. Genentech said it "admits that, based on the allegations, the Court has jurisdiction to hear this dispute." J.A. 149. City of Hope likewise made no jurisdictional objection. J.A. 183. The complaint also sought damages for federal and state antitrust and unfair-competition violations, based on collusion by Genentech and Celltech to obtain issuance of the Cabilly II patent and share in its benefits, J.A. 63-68, 141-48; those claims were dismissed on grounds of *Noerr-Pennington* immunity.[3] J.A. 349. The case moved towards trial. J.A. 24.

Then, on March 5, 2004, the United States Court of Appeals fo the Federal Circuit decided *Gen-Probe Inc.* v. *Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir.), *pet'n for cert. dismissed*, 543 U.S. 941 (2004). *Gen-Probe* held that a patent licensee seeking a declaratory judgment "must . . . materially breach the agreement . . . before bringing suit," 359 F.3d at 1381, and that as a matter of law, when a patent licensee continued to pay royalties and did not violate the license, "no actual controversy supports jurisdiction under the Declaratory Judgment Act," *id.* at 1382.

The District Court (Pfaelzer, J.) granted motions by Genentech and City of Hope to dismiss for lack of subject-matter jurisdiction. P.C.A. 31a. The court explained that it

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[3] See *Eastern R.R. Presidents Conference* v. *Noerr Motor Freight, Inc.*, 365 U.S. 127 (1961); *United Mine Workers* v. *Pennington*, 381 U.S. 657 (1965). Judgment on those claims was entered under Fed. R. Civ. P. 54(b), J.A. 380, and separately appealed, J.A. 381. Celltech was a party in the courts below with respect to those claims; it is not a party in this Court.

had "no choice but to dismiss" because "*Gen-Probe* held that a licensee in good standing cannot seek relief under the Declaratory Judgment Act." P.C.A. 28a. At the same time, the District Court observed that it dismissed with reluctance:

> "Even if it has serious misgivings about the panel's conclusion, this Court is not free to reconsider policy ramifications that *Gen-Probe* rejected."

P.C.A. 31a. The District Court characterized the Federal Circuit's new doctrine as a departure from that circuit's and this Court's previous rulings:

> "In the past, the 'actual controversy' requirement has not been interpreted as precluding a licensee from challenging a patent it licenses. *See C.R. Bard Inc. v. Schwartz*, 716 F.2d 874, 875 (Fed. Cir. 1983) ('[A] patent license need not be terminated before a patent licensee may bring a declaratory judgment action'); *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969) (holding that a license does not bar the licensee from challenging the validity of the patent)."

P.C.A. 24a. The District Court added that "The public has a strong interest in ferreting out invalid or unenforceable patents," P.C.A. 30a, and it quoted this Court:

> "Surely the equities of the licensor do not weigh very heavily when they are balanced against the important public interest in permitting full and free competition in the use of ideas which are in reality a part of the public domain."

*Id.*, quoting *Lear*, 395 U.S. at 670. But, obeying *Gen-Probe*, the District Court dismissed, while expressing concern that the Federal Circuit's doctrine "forces licensees to take a tremendous risk to challenge a patent, one that some with valid claims will likely be unwilling to take." P.C.A. 30a.

### F. The Court of Appeals Decision.

On appeal the Federal Circuit (Newman, J., joined by Mayer and Clevenger, JJ.) affirmed the dismissal, following its jurisdictional rule stated in *Gen-Probe* and reiterated in

*MedImmune, Inc.* v. *Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005), *pet'n for cert. pending*, No. 05-656. P.C.A. 1a.[4] The court held that because MedImmune had continued to pay, albeit under protest, the royalties demanded by Genentech, therefore as a matter of law MedImmune could not have a "reasonable apprehension . . . that it will face an infringement suit," P.C.A. 7a, and therefore there could be no "actual controversy" satisfying "the constitutional and statutory requirements," P.C.A. 7a-8a. In order to constitute an "actual controversy," the Federal Circuit held,

> "there must be both (1) a reasonable apprehension on the part of the declaratory judgment plaintiff that it will face an infringement suit, and (2) present activity by the declaratory judgment plaintiff which could constitute infringement . . . ."

P.C.A. 7a, quoting *MedImmune, Inc.* v. *Centocor, Inc.*, 409 F.3d at 1379. To permit a declaratory-judgment action, the court believed, would create an "inequity" that would permit the licensee to sue but retain its rights under the license if it lost. P.C.A. 7a.

The Court of Appeals devoted one paragraph to putting aside this Court's decisions construing the Declaratory Judgment Act. P.C.A. 8a. The Court of Appeals also rejected the pertinence of this Court's decision in *Lear, Inc.* v. *Adkins*, which had held that federal patent policy strongly encourages the testing of patent claims, and that a licensee could not be estopped to challenge the validity of a licensed patent. *Lear*, the court said, did not apply because there the patent licensee had stopped paying royalties under the license. P.C.A. 4a-6a. "[T]he issue here is not one of estoppel, but of availability of the declaratory judgment procedure." P.C.A. 6a.

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[4] The Court of Appeals also affirmed summary judgment on the antitrust and unfair-competition claims based on *Noerr-Pennington* immunity. P.C.A. 11a-12a. Judge Clevenger dissented from that part of the decision, reasoning that the appeal of that judgment should have been transferred to the Ninth Circuit pursuant to 28 U.S.C. § 1631. P.C.A. 17a-20a.

The Court of Appeals similarly found no useful guidance in this Court's admonition in *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83, 100, 102 (1993), that the policy enacted in the patent code favors adjudication of the validity of patents, and that validity should be decided under the Declaratory Judgment Act even after a finding of non-infringement, *id.* at 96. Because *Cardinal Chemical* "was an infringement suit, not a declaratory action," the Court of Appeals concluded that "the present case is unaffected by *Cardinal Chemical*." P.C.A. 8a.

## SUMMARY OF ARGUMENT

One would have thought that the issue in this case had been settled for almost seventy years. In 1934, encouraged by a unanimous 1933 decision of this Court holding that Article III embraces declaratory judgments in actual, concrete legal controversies,[5] Congress with the support of academics, business enterprises and the bar enacted the Declaratory Judgment Act, now 28 U.S.C. § 2201. A very simple provision, the Act authorizes a federal court to issue a judgment declaring legal rights in a "case of actual controversy." The Act was adopted so that in such a case it would not be "necessary to breach a contract or a lease, or act upon one's own interpretation of his rights when disputed;" instead, under the Declaratory Judgment Act "it is not necessary to bring about such social and economic waste and destruction in order to obtain a determination of one's rights." S. Rep. No. 1005, 73d Cong., 2d Sess. 3 (1934).

The Act soon was applied by this Court in three leading cases. In *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227, 241 (1937), this Court held unanimously that the Act and Article III required simply "a concrete case admitting of an immediate and definitive determination of the legal rights of the parties in an adversary proceeding." In *Maryland Cas.*

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[5] *Nashville, C. & St. L. Ry.* v. *Wallace*, 288 U.S. 249 (1933).

*Co.* v. *Pacific Coal & Oil Co.*, 312 U.S. 270, 273 (1941), again unanimously, this Court described "the question in each case" as whether there is "a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality." And in *Altvater* v. *Freeman*, 319 U.S. 359, 364 (1943)—a challenge to the validity of a patent, brought by licensees paying royalties—this Court held that "[t]he fact that royalties were being paid" did not affect jurisdiction. This Court later summarized, also without dissent, that "[t]he sole requirement for jurisdiction under the Act" is that there be a "real and immediate . . . actual 'controversy.'" *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83, 96 (1993), quoting *Arrowhead Indus. Water, Inc.* v. *Ecolochem, Inc.*, 846 F.2d 731, 735 (Fed. Cir. 1988).

Nevertheless, in a recent series of jarring decisions, of which this is the latest, the Federal Circuit has paid little heed to this Court's holdings and has ignored the central purpose of the Declaratory Judgment Act. The Federal Circuit holds that under Article III and the Act, a manufacturer accused by a patentee of liability under a license for an assertedly infringing product cannot seek a declaratory judgment unless it first commits material breach of the license by refusing to pay royalties—thereby placing itself in jeopardy not only of damages for breach of contract, but of an injunction prohibiting sales of its product, treble-damage penalties, interest, attorneys' fees and other costly sanctions for patent infringement under 35 U.S.C. §§ 283, 284 and 285. That absolute rule has no support in the statute's text or history, nor in this Court's precedents.

That new constitutional interpretation would have amazed the drafters of the Declaratory Judgment Act—whose purpose, expressed in a simple, encompassing text and unambiguous explanations by the enactors—was to allow contracting parties to resolve their disputes in court without breach and without risking economic destruction and multiplying damages. The Act, as often recognized and reiterated, was

designed to permit judicial resolution of contract disputes "before or after breach." REPORT OF ADVISORY COMMITTEE ON RULES FOR CIVIL PROCEDURE 145 (1937). That has long been settled law throughout the country. The holding here, besides disregarding decades of contrary appellate decisions and the understanding of leading treatise writers, would on unsupported constitutional grounds disrupt the law of licenses and contracts throughout the economy, essentially undoing the achievement of the reformers of 1934.

Apart from its constitutional error and disregard of precedent, the Federal Circuit also is entirely at odds with a century of decisions of this Court applying federal patent law. This Court repeatedly has emphasized that the patent laws enacted by Congress *favor* and *encourage* and *protect* challenges to patent validity. See *Cardinal Chemical*, 508 U.S. at 100; *Blonder-Tongue Labs.* v. *University of Ill. Foundation*, 402 U.S. 313, 344-45 (1971). This Court has recognized that a licensee often will be the most likely and effective challenger to an invalid patent. *Lear, Inc.* v. *Adkins*, 395 U.S. 653, 670 (1969). Yet the Federal Circuit holds that by agreeing to a license—in this case, a license including a broad patent not issued and its claims not disclosed until four years later—the licensee is paralyzed from challenging a patentee's assertion of liability, unless it is willing to jeopardize its principal product, and risk potential financial ruin if a preliminary injunction is entered or its case does not succeed.

The Federal Circuit, citing its own policy judgments, would revive for patent licensees not in breach the discredited doctrine of licensee estoppel, which this Court emphatically rejected in *Lear*. Further, it would write that new barrier into Article III of the Constitution, beyond the corrective power of Congress—the body assigned by Article I to adjust patent policy.

## ARGUMENT

### I. THE COMPLAINT STATED A "CASE OF ACTUAL CONTROVERSY" UNDER THE DECLARATORY JUDGMENT ACT AND ARTICLE III.

The Declaratory Judgment Act has been a useful part of the federal judicial code for more than seventy years. Enacted in 1934, its text provides:

> "In a case of actual controversy within its jurisdiction [with specified exceptions] . . . any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested party seeking such declaration, whether or not further relief is or could be sought. . . ."

28 U.S.C. § 2201(a). The Act, it has been recognized since its beginning, reaches to the full scope of the federal judicial power of Article III. *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227, 239-40 (1937); *Ashwander* v. *TVA*, 297 U.S. 288, 325 (1936).

#### A. The Declaratory Judgment Act and Article III Do Not Exclude Patent Licensees Paying Royalties Under Protest.

##### 1. *A "Case of Actual Controversy" Is a Concrete Legal Dispute Between Parties With Adverse Interests.*

***(a) Early Decisions.—Aetna Life Ins. Co. v. Haworth.***— The requirements for a "case of actual controversy" under the 1934 Act were soon explained by this Court unanimously through Chief Justice Hughes:

> "A justiciable controversy is . . . *distinguished from* a difference or dispute of a *hypothetical or abstract* character; from one that is academic or moot. . . . The controversy *must be definite and concrete*, touching the

> legal relations of parties having *adverse legal interests*. . . . It must be *a real and substantial controversy admitting of specific relief* through a decree of a conclusive character, as distinguished from an opinion advising what the law would be upon a hypothetical state of facts."

*Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227, 240-41 (1937) (emphasis supplied). In *Aetna*, a policyholder of five life insurance policies gave notice that he was permanently disabled and so entitled to benefits under two of them, and also that he was no longer obliged to pay premiums but that the insurance company would be liable at his death. Although the company refused to recognize his claims, he did not bring suit. *Id.* at 238. The insurance company then sought relief under the Declaratory Judgment Act, alleging that without a resolution of the dispute, evidence might be lost, and that it would need to set aside a reserve for potential liability. *Id.* at 239. This Court held that the requirements of the Act and the Constitution were satisfied. The complaint "calls, not for an advisory opinion upon a hypothetical basis, but for an adjudication of present right upon established facts." *Id.* at 242. This Court reaffirmed, as it had in *Nashville, C. & St. L. Ry.* v. *Wallace*, 288 U.S. 249 (1933), that what Article III requires is

> "a concrete case admitting of an immediate and definitive determination of the legal rights of the parties in an adversary proceeding."

*Aetna*, 300 U.S. at 241—a dispute that "is definite and concrete, not hypothetical or abstract," *id.* at 242.

***Maryland Casualty.***—Four years after *Aetna* this Court emphasized that the Declaratory Judgment Act prescribes no rigid or mechanical formula for a "case of actual controversy," as long as the essentials of a concrete, adversarial legal dispute are present. In language often quoted since, this

Court held that the Act calls for examing the particular circumstances:

> "The difference between an abstract question and a 'controversy' contemplated by the Declaratory Judgment Act is necessarily one of degree, and it would be difficult, if it would be possible, to fashion a precise test for determining in every case whether there is such a controversy. Basically, the question in each case is whether the facts alleged, under all the circumstances, show that there is a *substantial controversy*, between parties having *adverse legal interests*, of *sufficient immediacy and reality* to warrant the issuance of a declaratory judgment."

*Maryland Cas. Co.* v. *Pacific Coal & Oil Co.*, 312 U.S. 270, 273 (1941).

***Altvater v. Freeman.***—Completing the trilogy of this Court's foundational decisions construing the Declaratory Judgment Act was a case like this one—a declaratory claim of patent invalidity by patent licensees paying royalties. *Altvater* v. *Freeman*, 319 U.S. 359 (1943), decided the same jurisdictional issue before this Court today. The petitioners, patent licensees in good standing who were sued for making unauthorized sales, filed a counterclaim for a declaratory judgment that the licensed patents were invalid. The licensees did not "cancel[] the license agreement" or "refuse[] to pay any royalties under it," because if they did "they would be subject to infringement suits." *Id.* at 361. Just as here, the patentee-licensors denied that there was an "actual controversy," arguing that "so long as they continue to pay royalties, there is only an academic, not a real controversy, between the parties." *Id.* at 364. This Court squarely rejected that argument:

> "The fact that royalties were being paid did not make this a 'difference or dispute of a hypothetical or abstract character.' *Aetna* . . . . That controversy was 'definite

> and concrete, touching the legal relations of parties having adverse legal interests.' *Aetna* . . . ."

*Id.* This Court emphasized that if the royalties, which were paid "under protest and under the compulsion of an injunction decree," had not been paid, the licensees faced a "risk . . . [of] treble damages in infringement suits." *Id.* at 365. They sought a declaratory judgment "to lift the heavy hand of that [royalty] tribute from the business." *Id.*

> "It was the function of the Declaratory Judgments Act to afford relief against such peril and insecurity . . . . And certainly the requirements of case or controversy are met where payment of a claim is demanded as of right and where payment is made, but where the involuntary or coercive nature of the exaction preserves the right to recover the sums paid or to challenge the legality of the claim."

*Id.* Further, this Court later explained that in *Altvater* "we nowhere stated that a [licensee] counterclaimant could seek the affirmance of a declaratory judgment only if it ensured that its future actions would continue to violate the patentee's alleged rights." *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83, 100 n.22 (1993).

Contemporaneous decisions authored by distinguished appellate judges underscored the seminal holdings of this Court. Six months after *Aetna*, Judge Parker explained that the Declaratory Judgment Act was enacted "to settle legal rights and remove uncertainty and insecurity from legal relationships without awaiting a violation of the rights or a disturbance of the relationships." *Aetna Cas. & Sur. Co.* v. *Quarles*, 92 F.2d 321, 325 (4th Cir. 1937). Judge Magruder wrote that "[t]his constitutional requirement [Article III], as applied to declaratory judgments, is not interpreted in any narrow or technical sense." *Dewey & Almy Chem. Co.* v. *American Anode, Inc.*, 137 F.2d 68, 70 (3d Cir.), *cert. denied*, 320 U.S. 761 (1943). Judge Swan explained that if a patent licensee were required to terminate the contract before seek-

ing declaratory judgment, "it will be too late to avoid an action for damages," yet "[t]he very purpose of the declaratory judgment procedure is to prevent the accrual of such avoidable damages," *American Machine & Metals, Inc.* v. *De Bothezat Impeller Co.*, 166 F.2d 535, 536 (2d Cir. 1948). Rather than requiring a licensee to "risk an otherwise profitable business in order to present a justiciable 'controversy[,]' [t]he Declaratory Judgments Act was designed to obviate just this sort of peril." *Id.* at 537.

***(b) Subsequent Decisions.***—This Court in later decisions explained that a dispute as to whether one is under a legal obligation with which one must comply is a classic "actual controversy": "if appellants are now under such an obligation, that in and of itself makes their attack on the validity of the law a live controversy, and not an attempt to obtain an advisory opinion." *Lake Carriers' Ass'n* v. *MacMullan*, 406 U.S. 498, 507 (1972). What matters is that—as here—

> "[t]he disagreement must not be nebulous or contingent but must have taken on fixed and final shape so that a court can see what legal issues it is deciding, what effect its decision will have on the adversaries, and some useful purpose to be achieved in deciding them."

*Public Serv. Comm'n* v. *Wycoff Co.*, 344 U.S. 237, 244 (1952). In *Cardinal Chemical* this Court confirmed that "a party may . . . seek a declaratory judgment, even if the patentee has not filed an infringement action," and held that Article III jurisdiction persisted on appeal "as long as the parties continued to dispute the issue of validity." 508 U.S. at 95, 97.

The regional courts of appeals when they had jurisdiction of patent cases held on several occasions that a "case of actual controversy" under the Declaratory Judgment Act does not require a patent licensee to withhold royalties or terminate a license. Otherwise the licensee would be forced to

> "sit back and continue to wonder if it is justly paying royalties or merely paying a bribe to the patentee not to

> threaten him with business disruption and a possible damage suit if he terminates royalty payments."

*Precision Shooting Equip. Co.* v. *Allen*, 646 F.2d 313, 318 (7th Cir.), *cert. denied*, 454 U.S. 964 (1981). The Second Circuit held that

> "Addressing the question whether a patent licensee must actually withhold royalty payments before he can challenge validity, we conclude—as have most courts who have considered the issue—that such *repudiation of the licensing agreement should not be precondition to suit*."

*Warner-Jenkinson Co.* v. *Allied Chem. Corp.*, 567 F.2d 184, 187 (2d Cir. 1977) (emphasis supplied). "There is clearly a case and controversy here since the plaintiffs-licensees have an interest in proving patent invalidity and thereby escaping liability for royalties." *Id.* at 187 n.4. *Accord*, *American Sterilizer Co.* v. *Sybron Corp.*, 526 F.2d 542, 543 (3d Cir. 1975). The Moore treatise summarized:

> "In general, the fact that a declaratory relief plaintiff holds a valid license to use the allegedly patented item is irrelevant; the licensee need not terminate the license in order to maintain a federal declaratory relief action for patent invalidity."

12 J. MOORE *et al.*, MOORE'S FEDERAL PRACTICE § 57.22[8][c][i] at 57-80 (3d ed. 2005).

The jurisdictional principle of course is not confined to patent licenses. For instance, a "licensee need not terminate its license agreement in order to maintain a federal declaratory action for copyright invalidity." *Hal Roach Studios, Inc.* v. *Richard Feiner & Co.*, 896 F.2d 1542, 1556 n.23 (9th Cir. 1990). Parties to all kinds of contracts are permitted to bring declaratory-judgment actions without first committing material breaches. "[A] party to a contract is not compelled to wait until he has committed an act which the other party

asserts will constitute a breach, but may seek relief by declaratory judgment and have the controversy adjudicated in order that he may avoid the risk of damages or other untoward consequence." *Keener Oil & Gas Co.* v. *Consolidated Gas Utilities Corp.*, 190 F.2d 985, 989 (10th Cir. 1951). Last year the Second Circuit "easily rejected" a challenge to declaratory jurisdiction when parties not in breach disputed the scope of coverage of an insurance policy. *Duane Reade, Inc.* v. *St. Paul Fire & Marine Ins. Co.*, 411 F.3d 384, 389 (2d Cir. 2005). In a suit challenging liability on a commercial lease, the same court held:

> "We agree with the plaintiff's implicit premise that it need not fail to make payments in violation of its lease or mortgage obligations in order to have a justiciable controversy concerning its obligation to make such payments."

*118 East 60th Owners, Inc.* v. *Bonner Properties, Inc.*, 677 F.2d 200, 202 n.1 (2d Cir. 1982). "The Declaratory Judgment Act exists to allow litigants to determine an actual controversy . . . before the dispute grows into a contract violation . . . ." *Doody* v. *Ameriquest Mortgage Co.*, 242 F.3d 286, 288 (5th Cir. 2001).[6]

### 2. *The Federal Circuit Disregarded the Decisions of This Court.*

The Federal Circuit offered no convincing way to escape the declaratory-judgment holdings of this Court. In *Gen-Probe* it had acknowledged this Court's *Aetna* decision but denied its authority on this basis:

> "While this language [in *Aetna*] suggests that a litigant may sue to determine contract rights before a breach, this 1937 Supreme Court case did not involve a de-

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[6] See also, *e.g.*, *Venator Group Specialty, Inc.* v. *Matthew/Muniot Family, LLC*, 322 F.3d 835, 840 (5th Cir. 2003); *Continental Cas. Co.* v. *Coastal Sav. Bank*, 977 F.2d 734, 738 (2d Cir. 1992).

> claratory judgment action instituted by a patent licensee in good standing."

359 F.3d at 1382. But "this 1937 Supreme Court case" stated a fundamental constitutionally-based rule of general application. There is no separate constitutional rule for patent-license cases that specially limits a federal court's jurisdiction under the Declaratory Judgment Act and Article III.

The Federal Circuit in the present case acknowledged *Maryland Casualty*, P.C.A. 8a, which looked to whether "under all the circumstances" there was a "substantial controversy" with "immediacy and reality" between parties with "adverse legal interests," 312 U.S. at 273. But the Federal Circuit, to the contrary, has announced an absolute rule that no "actual controversy" can exist without breach of contract. It maintained that its automatic rule was not a departure from *Maryland Casualty*, but simply a "synthesis of the totality-of-the-circumstances test for determining whether there is a justiciable controversy." P.C.A. 7a-8a.

The Federal Circuit here made no mention of *Altvater*, which approved a declaratory-judgment claim by patent licensees not in breach. In *Gen-Probe* (which was settled soon after a petition for certiorari was filed) the Federal Circuit had held *Altvater* inapplicable because "[t]he royalty payments in *Altvater* were paid not under the terms of a license agreement; rather, they were paid 'under the compulsion of an injunction decree,'" 359 F.3d at 1382, quoting *Altvater*, 319 U.S. at 365—even though this Court in *Altvater* had equally noted that, as here, the royalties also were paid "under protest," 319 U.S. at 365, and this Court explicitly held that ongoing royalty payments and absence of breach did not preclude an "actual controversy" under the Declaratory Judgment Act. *Id.*

*Cardinal Chemical* was previously dismissed by the Federal Circuit as a decision that "did not concern the jurisdiction of federal district courts" (as opposed to appellate courts) and

therefore was "inapposite," and should be "limited to the specific facts of that case." *MedImmune, Inc.* v. *Centocor, Inc.*, 409 F.3d at 1380, quoting in part *Lamb-Weston, Inc.* v. *McCain Foods, Ltd.*, 78 F.3d 540, 546 (Fed. Cir. 1996). In the present case once again the Federal Circuit concluded that "nothing in *Cardinal* undermines our decisions on declaratory justiciability at the trial court level." P.C.A. 8a, quoting *Super Sack Mfg. Corp.* v. *Chase Packaging Corp.*, 57 F.3d 1054, 1060 (Fed. Cir. 1995). It has called *Cardinal Chemical*'s applicability "twice rejected" by its own prior decisions, *MedImmune*, 409 F.3d at 1380, and held that "[t]he present case is unaffected by *Cardinal Chemical*." P.C.A. 8a.

### B. This Is a "Case of Actual Controversy."

The judgment on review here endorses a rule that as a matter of law there can be no "actual controversy" in a patent challenge by a licensee unless the licensee has a "reasonable apprehension of suit"—and that, also as a matter of law, as long as royalties are being paid and no breach has occurred, "reasonable apprehension of suit" cannot exist.[7] The statute, however, speaks of "case of actual controversy." The phrase "reasonable apprehension of suit" is not to be found in the text or history of the statute, nor has this Court ever used it.

> "The sole requirement for jurisdiction under the Act is that the conflict be real and immediate, i.e., that there be a true, actual 'controversy' required by the Act."

*Cardinal Chemical*, 508 U.S. at 96, quoting *Arrowhead Indus. Water, Inc.* v. *Ecolochem, Inc.*, 846 F.2d 731, 734-35 (Fed. Cir. 1988). However, under either formulation—"actual controversy" or "reasonable apprehension of suit"—the Act is satisfied here.

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[7] In one case the Federal Circuit escalated its requirement to "reasonable apprehension of *imminent* suit." *Teva Pharmaceuticals USA, Inc.* v. *Pfizer, Inc.*, 395 F.3d 1324, 1333 (Fed. Cir.) (emphasis in original), *cert. denied*, 126 S. Ct. 473 (2005).

### 1. *"Actual Controversy" Is Not Limited to "Reasonable Apprehension of Suit."*

"Reasonable apprehension of suit" first appeared in the context of the typical action for declaration of invalidity and non-infringement brought by a potential infringer against a patentee. In such suits "reasonable apprehension of suit," along with likelihood of producing the disputed item (here already produced and sold for four years) could establish a concrete legal controversy. See *Société de Conditionnement* v. *Hunter Engineering Co.*, 655 F.2d 938, 944 (9th Cir. 1981); *Japan Gas Lighter Ass'n* v. *Ronson Corp.*, 257 F. Supp. 219, 237 (D.N.J. 1966).

A "reasonable apprehension of suit" certainly can be significant, and often may be *sufficient* in the circumstances to establish an "actual controversy." But apprehension of suit is not a *necessary* condition, and this Court has never suggested such a thing. It scarcely would have, given that in *Aetna* this Court noted that the plaintiff was suing precisely *because* the adverse party had declined to bring its asserted claim to court; the insurance company properly sought a declaratory judgment when the insured and beneficiary

> "have not instituted any action wherein the plaintiff would have an opportunity to prove the absence of the alleged disability."

300 U.S. at 239.

Courts of appeals have confirmed that apprehension of a lawsuit "is not the only way to establish the existence of a case for purposes of Article III." *Sallen* v. *Corinthians Licenciamentos LTDA*, 273 F.3d 14, 25 (1st Cir. 2001). In *Precision Shooting*, 646 F.2d at 314, the Seventh Circuit recognized that an "actual controversy" existed even if a patent licensee paying royalties had "no reasonable apprehension of liability in an infringement suit." The appropriate

question, the court held, was whether there was "a reasonable apprehension that the patentee will bring an infringement suit against [the licensee] *if there is non-compliance with the license*." 646 F.2d at 318 (emphasis supplied). This Court explained:

> "If . . . a party has actually been charged with infringement of the patent, there is, *necessarily*, a case or controversy adequate to support jurisdiction of a complaint . . . under the Act."

*Cardinal Chemical*, 508 U.S. at 96 (emphasis in original). This Court in *Cardinal Chemical* further observed that an "actual controversy" under the Declaratory Judgment Act could include a challenge to a patent's validity even without a prior charge of infringement:

> "Merely the desire to avoid the threat of a 'scarecrow' patent, in Learned Hand's phrase, may therefore be sufficient to establish jurisdiction under the Declaratory Judgment Act."

*Id.* (footnote omitted), quoting *Bresnick* v. *United States Vitamin Corp.*, 139 F.2d 239, 242 (2d Cir. 1943). See also *Hanes Corp.* v. *Millard*, 531 F.2d 585, 592 (D.C. Cir. 1976).

Certainly payment under protest, as occurred here, does not negate an "actual controversy" under the Act. See *Altvater*, 319 U.S. at 365. This Court never has abided the argument that a payment made under threat of financial ruin is voluntary and waives judicial relief. As explained through Justice Holmes,

> "It always is for the interest of a party under duress to choose the lesser of two evils. But the fact that a choice was made according to interest does not exclude duress. It is the characteristic of duress properly so called."

*Union P.R.R.* v. *Public Serv. Comm'n*, 248 U.S. 67, 70 (1918). See also, *e.g.*, *Swift Co.* v. *United States*, 111 U.S. 22, 28-29 (1884) ("The appellant had no choice. The only

alternative was to submit to an illegal exaction, or discontinue its business."); *Atchison, T. & S.F. Ry.* v. *O'Connor*, 223 U.S. 280, 286-87 (1912) (Holmes, J.) (when party paying tax "had no certainty of ultimate success," and chose not "to take the risk of having its contracts disputed and its business injured and of finding the tax more or less nearly doubled," then "the payment was made under duress").

**2. *Petitioner Presented an "Actual Controversy."***

The statutory requirements are satisfied here. The court acknowledged that the parties had "adverse legal interests." P.C.A. 8a, quoting *Aetna*, 300 U.S. at 241. The dispute was as to the parties' "rights and other legal relations." 28 U.S.C. § 2201(a). And there was an "actual controversy within its jurisdiction," in which the material facts are concrete rather than speculative, and a court ruling can resolve the dispute. That statutory template is not affected by whether in addition MedImmune "take[s] some additional act to deepen gray into black," *Precision Shooting*, 646 F.2d at 318, by putting itself in breach of the license agreement to which Genentech asserted it was subject.

A central concern when Article III was first applied to declaratory judgments was that the facts and issues be actual, adverse and concrete. *Nashville Ry.*, 288 U.S. at 264; *Aetna*, 300 U.S. at 240-41. MedImmune was not a stranger with no interest. Here the uncontroverted record shows a specific assertion of liability based on infringement of a patent by sales of a product approved by the FDA and on the market; a demand for royalties; denial of infringement and liability; denial of the validity and enforceability of the patent; and payment under protest. For MedImmune to commit breach of the license would not make this case any more concrete and "admitting of an immediate and definitive determination of the legal rights of the parties." *Aetna*, 300 U.S. at 241. All that breach would accomplish would be to heighten the risks

and consequences—exactly what the Declaratory Judgment Act was enacted to avoid.

This dispute fits easily within this Court's decisions. As in *Aetna*, it is a dispute about legal obligations that "is definite and concrete, not hypothetical or abstract." 300 U.S. at 242. As in *Maryland Casualty*, it is "a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality." 312 U.S. at 273. And if the Federal Circuit decision here is correct, *Altvater* could not have been decided as it was.

### 3. *Petitioner Presented a "Reasonable Apprehension of Suit."*

Even if "reasonable apprehension of suit," rather than "actual controversy" were the only constitutional and statutory test, the undisputed facts here amply demonstrated not only an "actual controversy," but a "reasonable apprehension of suit" as well.[8]

Beginning in the 1930s, countless decisions have allowed declaratory-judgment actions by manufacturers which have been accused by a patentee of infringement, but have not been sued for it. Those cases have held that such accusation creates a "reasonable apprehension of suit" sufficient for an "actual controversy." That assertion of infringement is exactly what occurred here, with Genentech also asserting that therefore Synagis® upon the issuance of the Cabilly II patent in 2001 became a "Licensed Product" that "would, if not licensed under this Agreement, infringe," J.A. 399, so that royalties were due under the 1997 license. J.A. 419, 428. MedImmune did not agree, and paid royalties only "under

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[8] The Court of Appeals incorrectly stated that "MedImmune concedes that it is free of apprehension of suit." P.C.A. 4a. MedImmune specifically declared, J.A. 389, and argued in the Court of Appeals that "Genentech's demands for royalties under an existing license for a new patent created a reasonable apprehension of an infringement suit." Brief of Plaintiff-Appellant, U.S. Ct. Apps., Fed. Cir., at 30.

protest." J.A. 389, 426. Genentech did not deny its "clear threat to enforce the Cabilly II patent against MedImmune." J.A. 388; see pp. 6-7, *supra*. MedImmune sought a declaration that Synagis® did not infringe, that it therefore was not covered by the license, and that the Cabilly II patent was both invalid and unenforceable. J.A. 60-63, 136-41. It was exactly "to lift the heavy hand of . . . tribute" without having to defend infringement actions that the Declaratory Judgment Act was enacted. *Altvater*, 319 U.S. at 365. The communications here went well beyond the minimum for "reasonable apprehension of suit;" "[t]he [patentee's] claim need not be formally asserted; it is not necessary that notice be given directly to the plaintiff or that any threat be made to sue the plaintiff." *Aralac, Inc.* v. *Hat Corp.*, 166 F.2d 286, 292 (3d Cir. 1948); see also *Dewey & Almy Chem. Co.* v. *American Anode, Inc.*, 137 F.2d 68, 70 (3d Cir.), *cert. denied*, 320 U.S. 761 (1943).

The Federal Circuit not only mistakenly narrowed the statute's "actual controversy" to "reasonable apprehension of suit." The court also assumed that Synagis® was a "Licensed Product" under the contract, which would be so only if it infringed the Cabilly II patent. The court then redefined and narrowed apprehension of suit to require material breach of contract. Even the Federal Circuit's own prior holdings do not support this. *E.g.*, *Arrowhead Indus. Water*, 846 F.2d at 735, quoted in *Cardinal Chemical*, 508 U.S. at 96; *C.R. Bard, Inc.* v. *Schwartz*, 716 F.2d 874, 880 (Fed. Cir. 1983) ("We reject the blanket approach . . . that there can never be an apprehension of a federal infringement suit and thus no controversy when a license is still in effect."); *Cordis Corp.* v. *Medtronic, Inc.*, 780 F.2d 991, 994 (Fed. Cir. 1985) ("In *C.R. Bard* . . . this court held that a patent licensee may seek a federal declaratory judgment to declare a patent, subject to a

license, invalid without prior termination of the license."), *cert. denied*, 476 U.S. 1115 (1986).[9]

### C. A Requirement To Commit Breach of Contract Would Be Contrary to the Text and Purpose of the Declaratory Judgment Act.

Few familiar federal laws have a clearer text and legislative history than the Declaratory Judgment Act. Declaratory judgments were recognized in England in 1883[10] and in the United States by a New Jersey statute in 1915, followed by several other states.[11] A federal declaratory judgment act was first proposed in Congress in 1919, and bills were reintroduced thereafter. See Borchard, *The Federal Declaratory Judgments Act*, 21 VA. L. REV. 35, 36 (1936). During the 1920s, however, there had been uncertainty whether an action for declaratory relief, which some opinions addressing state laws suggested would amount to an "advisory opinion," could satisfy the requirements of Article III.[12] The constitutional doubt was dispelled in 1933 when this Court through Justice

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[9] See also *Teva Pharmaceuticals USA, Inc.* v. *Pfizer Inc.*, 405 F.3d 990, 997 (Fed. Cir.) (Dyk, J., dissenting as to rehearing *en banc*) ("In my view, the First Circuit [in *Sallen*, *supra*] is correct: the proper test under Article III is whether there is a present concrete controversy, and the panel here applied an incorrect test [reasonable apprehension of suit]."), *cert. denied*, 126 S. Ct. 473 (2005).

[10] Supreme Court of Judicature, Order XXV, § 5 (1883), 7 STATUTORY RULES AND ORDERS REVISED 54 (1904). See E. BORCHARD, DECLARATORY JUDGMENTS 129-130 (2d ed. 1941).

[11] N.J. Laws, 1915, ch. 116, § 7, called "the first effective statute" of this kind in a country. E. BORCHARD at 132. Professor Edwin Borchard was recognized as the "author of the Federal Declaratory Judgment Act." *Steffel* v. *Thompson*, 415 U.S. 452, 468 n.19 (1974). His treatise continues to be cited regularly in decisions construing the Act. *E.g.*, *Wilton* v. *Seven Falls Co.*, 515 U.S. 277, 288, 289 (1995).

[12] See E. BORCHARD at 134; *Willing* v. *Chicago Auditorium Ass'n*, 277 U.S. 274, 289 (1928); *Liberty Warehouse Co.* v. *Burley Tobacco Growers' Co-op. Marketing Ass'n*, 276 U.S. 71, 89 (1928).

Stone unanimously held that Article III did not stand in the way of reviewing a Tennessee declaratory judgment

> "so long as the case retains the essentials of *an adversary proceeding, involving a real, not a hypothetical, controversy*, which is finally determined by the judgment below."

*Nashville, C. & St. L. Ry.* v. *Wallace*, 288 U.S. 249, 264 (1933) (emphasis supplied). Article III, this Court held, is satisfied

> "when the complainant asserts rights which are challenged by the defendant, and presents for decision an actual controversy to which he is a party, capable of final adjudication by the judgment or decree to be rendered."

*Id.* at 260. That explanation of what Article III requires cleared the way for enactment of the Declaratory Judgment Act the following year. See S. Rep. No. 1005, 73d Cong., 2d Sess. 5 (1934); *Public Serv. Comm'n* v. *Wycoff Co.*, 344 U.S. at 241-42.

### 1. *The Declaratory Judgment Act Was Adopted To Make Breach of Contract Unnecessary.*

To demand that a declaratory-judgment plaintiff first commit a contractual breach, risking injunction of its major product, substantial damages and penalties, is the last thing that Congress in 1934 thought it was doing. The Declaratory Judgment Act applies by its terms to a "case of actual controversy." 28 U.S.C. § 2201(a).[13] The express purpose of

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[13] Article III, § 2, extends the federal judicial power to *inter alia* "all Cases, in Law and Equity, arising under . . . the Laws of the United States" and "Controversies . . . between Citizens of different States." See also *Calderon* v. *Ashmus*, 523 U.S. 740, 746 (1998). The phrase "case of actual controversy" was borrowed from contemporaneous state declaratory-judgment statutes, *e.g.*, Kan. Laws, 1921, ch. 168, § 1 ("cases of actual controversy"); Cal. Stats., 1921, p. 689 (same); Va. Laws, 1922, p.

the Act was to authorize the adjudication of real and concrete disagreements without forcing a party first to put itself in jeopardy of paying damages or other penalties if its legal claim ultimately did not succeed. The Senate report quoted with approval a supporter in a previous Congress:

> "Under the present law you take a step in the dark and then turn on the light to see if you have stepped into a hole. Under the declaratory judgment law you turn on the light and then take the step."

S. Rep. No. 1005 at 3, quoting 69 CONG. REC. 2108 (1928) (Rep. Gilbert). See also Hearings on H.R. 5623 Before Subcomm. of Senate Comm. on Judiciary, 70th Cong., 1st Sess. 55 (1928) (letter of Chief Judge Benjamin N. Cardozo) ("useful expedient to litigants who would otherwise have acted at their peril, or at best would have been exposed to harrowing delay").

Contract disputes, of which patent-license controversies are a subset, were a primary focus of Congress when it enacted the Declaratory Judgment Act in 1934. Congress explained its purpose to

> "enable[] parties in disputes over their rights over a contract, deed, lease, will, or any other written instrument to sue for a declaration of rights, *without breach of the contract* . . . ."

S. Rep. No. 1005 at 2 (emphasis supplied). Citing states' experience, the drafters observed:

> "The [declaratory judgment] procedure has been especially useful in *avoiding the necessity*, now so often present, *of having to act at one's peril* or to act on one's own interpretation of his rights, or abandon one's rights because of a fear of incurring damages. . . . Persons now often have to act at their peril, a danger which could be

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902 (same). See Borchard, 21 VA. L. REV. at 44. "The word 'actual' is one of emphasis rather than of definition." *Aetna*, 300 U.S. at 240.

> frequently avoided by the ability to sue for a declaratory judgment as to their rights or duties."

*Id.* at 2-3 (emphasis supplied), quoted in *Steffel* v. *Thompson*, 415 U.S. 452, 480 n.1 (1974) (Rehnquist, J., concurring). See also, *e.g.*, *Abbott Labs.* v. *Gardner*, 387 U.S. 136, 152 (1967) (risk of potential penalties before adjudication was "a dilemma that it was the very purpose of the Declaratory Judgment Act to ameliorate").

The understanding from the beginning has been that the Declaratory Judgment Act "enable[s] a party who is challenged, threatened or endangered in the enjoyment of what he claims to be his rights, to initiate the proceedings against his tormentor and remove the cloud." *United States* v. *Doherty*, 786 F.2d 491, 498-99 (2d Cir. 1986) (Friendly, J.), quoting E. BORCHARD, DECLARATORY JUDGMENTS 280 (2d ed. 1941). One accused of patent infringement "should not be compelled to act at its peril when it has the foresight to seek declaratory relief." *Broadview Chem. Corp.* v. *Loctite Corp.*, 417 F.2d 998, 1001 (2d Cir. 1969), *cert. denied*, 397 U.S. 1064 (1970). "The purpose of the Declaratory Judgment Act is to enable parties to adjudicate their disputes before either suffers great damage." 12 J. MOORE *et al.* § 57.03[2] at 57-11; see also 5 C. WRIGHT *et al.*, FEDERAL PRACTICE & PROCEDURE § 1238 at 411 (3d ed. 2004).

To require breach of the contract as a condition to suit would not make the present dispute any more clear or concrete. But it would place petitioner in a "very real dilemma" and "quite clearly exposed to the imposition of strong sanctions." *Abbott Labs.*, 387 U.S. at 153, 154. "[T]he declaratory judgment procedure is an alternative to pursuit of the arguably illegal activity." *Steffel*, 415 U.S. at 480 & n.1 (Rehnquist, J., concurring). See also *Evers* v. *Dwyer*, 358 U.S. 202, 204 (1958) ("We do not believe that appellant, in order to demonstrate the existence of an 'actual controversy' over the validity of the statute here challenged, was bound to continue to ride the Memphis buses at the risk of arrest if he

refused to seat himself in the space in such vehicles assigned to colored passengers."); *Gardner* v. *Toilet Goods Ass'n*, 387 U.S. 167, 172 (1967) (alternative to declaratory-judgment action is "beset with penalties and other impediments").

Declaratory judgments, it has been noted, are particularly appropriate for patent litigation. *Hanes Corp.* v. *Millard*, 531 F.2d 585, 592 (D.C. Cir. 1976) ("indisputably appropriate"); *Société de Conditionnement*, 655 F.2d at 943 (same); The practical risks of being held liable for infringement are particularly serious. See 35 U.S.C. §§ 283 (injunction), 284 (treble damages), 285 (attorneys' fees). Absent prompt judicial resolution of disputes about patent validity and infringement, the licensee's only alternative is "to risk not only actual but treble damages in infringement suits . . . . It was the function of the Declaratory Judgments Act to afford relief against such peril and insecurity." *Altvater*, 319 U.S. at 365.

The enactments of the Declaratory Judgment Act also had in mind the situation in which

> "the plaintiff, desiring not to sunder the economic or social relations involved, which a 'fight to the finish' might entail, contents himself with a suit for a judgment declaring his rights in the premises, enabling him thus to proceed to adjust his established legal relations accordingly."

Borchard, 21 VA. L. REV. at 39. In *Gen-Probe*, for example, "Gen-Probe expressly acknowledged its desire to maintain the status quo and remain a faithful licensee. Moreover, Gen-Probe exercised options to extend the duration of the license . . . ." 359 F.3d at 1380. Similarly, in the present case petitioner in 2003 sought and negotiated with respondent Genentech licenses for additional products, even though the dispute concerning alleged infringement of the Cabilly II patent by Synagis® and its validity remained unresolved. See J.A. 429, 431, 433, 434, 437. "[T]he declaratory judgment . . .

enables litigants to . . . settle the controversy before an accumulation of differences and hostility has engendered a wide and general conflict, involving numerous collateral issues." S. Rep. No. 1005 at 3.

It would confound the goal of the Declaratory Judgment Act to hold, as the Federal Circuit did here, that petitioner needed to commit breach of contract and place itself in great jeopardy before seeking judicial resolution of a clear legal dispute. The whole purpose of the Act was to eliminate the need for such risk-taking, commercial uncertainty, and piling on of potential damages.

### 2. *Rule 57 Contemplates Declaratory Judgments "Before or After Breach."*

The same year *Aetna* was decided, this Court also adopted the new Federal Rules of Civil Procedure. Order, 302 U.S. 783 (1937). Rule 57, unchanged in substance today, provided for declaratory judgments. Order, 308 U.S. 645, 736 (1938). The distinguished Advisory Committee this Court appointed summarized concisely the requirements for seeking declaratory relief: the plaintiff "must have a practical interest in the declaration sought," which may be as to "[t]he existence or non-existence of any right, duty, power, liability, privilege, disability, or immunity or of any fact upon which . . . legal relations depend." REPORT OF THE ADVISORY COMMITTEE ON RULES FOR CIVIL PROCEDURE 145 (1937) (Rule 58, later renumbered 57). The Advisory Committee's explanation specified that in declaratory actions

> "Written instruments, including ordinances and statutes, may be construed *before or after breach* at the petition of a properly interested party . . . ."

*Id.* (emphasis supplied). Yet the Federal Circuit's recent decisions hold just the opposite—as if Rule 57 instead had meant, to the contrary, that "written instruments . . . may be construed *only after breach*." The Federal Circuit, unlike any

other, explicitly holds as an absolute rule that a licensee "must . . . materially breach the agreement . . . before bringing suit." *Gen-Probe*, 359 F.3d at 1381. The notion that a litigant must first commit breach of the contract at issue—negating the very purpose of the Rule and the Act—surely would have puzzled the drafters both of the Act and of the Rule.

## II. TO BAR PETITIONER FROM DECLARATORY RELIEF WOULD CONSTITUTIONALIZE THE REJECTED DOCTRINE OF LICENSEE ESTOPPEL.

The Federal Circuit's new jurisdictional holding would write into Article III of the Constitution a policy that this Court has repeatedly held the patent laws reject.

### A. *Pope Mfg. Co.* v. *Gormully* Rejected Contractual Prohibitions of Patent Challenges.

In 1892 this Court held that a licensee's promise in a patent license not to challenge the patent's validity would be unenforceable in equity, because the right to challenge a patent "is not only a private right to the individual, but it is founded on public policy." *Pope Mfg. Co.* v. *Gormully*, 144 U.S. 224, 235 (1892).

> "It is as important to the public that competition should not be repressed by worthless patents, as that the patentee of a really valuable invention should be protected in his monopoly . . . ."

*Id.* at 234. See also *Haughey* v. *Lee*, 151 U.S. 282, 285 (1894) ("relieve the public from an asserted monopoly"). Therefore a patent license could "not operate to estop the defendants from contesting the validity of these patents." *Pope Mfg. Co.* v. *Gormully & Jeffery Mfg. Co. (No. 4)*, 144 U.S. 254, 255 (1892).

Many decisions of this Court since 1892 have reiterated

> "the importance to the public at large of resolving questions of patent validity"

*Cardinal Chemical*, 508 U.S. at 100, citing *Blonder-Tongue Labs., Inc.* v. *University of Ill. Foundation*, 402 U.S. 313 (1971). "It is the public interest which is dominant in the patent system." *Mercoid Corp.* v. *Mid-Continent Investment Co.*, 320 U.S. 661, 665 (1944). "The possession and assertion of patent rights are 'issues of great moment to the public.'" *Precision Instrument Mfg. Co.* v. *Automotive Maintenance Machinery Co.*, 324 U.S. 806, 815 (1945), quoting in part *Hazel-Atlas Glass Co.* v. *Hartford-Empire Co.*, 322 U.S. 238, 246 (1944). Federal patent policy is generally to "encourage authoritative testing of patent validity," "eliminating obstacles to suit by those disposed to challenge the validity of a patent," *Blonder-Tongue*, 402 U.S. at 344-45 (citing cases), "keeping open the way for interested persons to challenge the validity of patents which might be shown to be invalid." *Edward Katzinger Co.* v. *Chicago Metallic Mfg. Co.*, 329 U.S. 394, 400 (1947). "[W]hat will usually be the better practice [is] inquiring fully into the validity of this patent." *Sinclair & Carroll Co.* v. *Interchemical Corp.*, 325 U.S. 327, 330 (1945), quoted in *Cardinal Chemical*, 508 U.S. at 100. See also *United States* v. *Glaxo Group Ltd.*, 410 U.S. 52, 57 (1973) (this Court has "repeatedly held that the private licensee-plaintiff in an antitrust suit may attack the validity of the patent under which he is licensed even though he has agreed not to do so in his license").[14]

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[14] The concern of the patent laws extends not just to the validity of the patent itself, but also to whether, as the complaint here alleged, J.A. 53-54, 137-40, the patent had been deceptively or fraudulently obtained. "The far-reaching social and economic consequences of a patent . . . give the public a paramount interest in seeing that patent monopolies spring from backgrounds free from fraud or other inequitable conduct and that such monopolies are kept within their legitimate scope." *Walker Process*

The Federal Circuit's holding that a license *per se* prevents an accused infringer not in breach from challenging patent validity is irreconcilable with *Pope Mfg. Co.* v. *Gormully* and a century of this Court's patent decisions. The Federal Circuit would imply as a matter of law a contract provision against challenging validity which not only was entirely absent here,[15] but would have been void and unenforceable if it had been present.

### B. *Lear, Inc.* v. *Adkins* Rejected Barring Suits by Patent Licensees.

In *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969), this Court through Justice Harlan rejected the doctrine of "licensee estoppel" as "inconsistent with the aims of federal patent policy." 395 U.S. at 673. The patent code, in 35 U.S.C. §§ 101, 102, 103 and 112, prescribes standards of utility, novelty, non-obviousness and specificity required for a patent to be valid. But the PTO, with limited staff and resources and a flood of applications, and acting *ex parte*, is in no position to assure that the statutory limitations always are honored. See FEDERAL TRADE COMM'N, TO PROMOTE INNOVATION, Exec. Sum. at 8-9, ch. 5 at 5-6 (2003) ("FTC Report"). "If [licensees] are muzzled, the public may continually be required to pay tribute to would-be monopolists without need or justification." *Lear*, 395 U.S. at 670; see also *Panther Pumps & Equip. Co.* v. *Hydrocraft, Inc.*, 468 F.2d 225, 231 (7th Cir. 1972) (Stevens, J.) (after *Lear*, "the 'no contest' provision in the LEMCO license is plainly unenforceable"), *cert. denied*, 411 U.S. 965 (1973).

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*Equip., Inc.* v. *Food Machinery & Chem. Corp.*, 382 U.S. 172, 177 (1965), quoting *Precision Instrument*, 324 U.S. at 816.

[15] The license contract in fact provided that royalties would not be due on any patent held invalid, and Genentech disclaimed any warranty. J.A. 399, 411.

For the same reasons, it was recognized soon after *Lear* that a promise not to challenge patent validity is unenforceable when contained in a settlement agreement. *Business Forms Finishing Service, Inc.* v. *Carson*, 452 F.2d 70, 73-75 (7th Cir. 1971) (Stevens, J.). The Federal Circuit, however, has not shared that view. Thus the Federal Circuit held in *Flex-Foot, Inc.* v. *CRP, Inc.*, 238 F.3d 1362, 1368 (Fed. Cir. 2001), that *Lear*'s "holding with respect to licensee estoppel is meaningfully distinguishable from the present case concerning a settlement agreement." See also *Diversey Lever, Inc.* v. *Ecolab, Inc.*, 191 F.3d 1350, 1352 (Fed. Cir. 1999) (permitting agreement in consent decree not to challenge patent validity).

Indeed, the Federal Circuit long has expressed and demonstrated hostility to *Lear*. It has characterized *Lear* as sounding "tones that echo from a past era of skepticism over intellectual property principles." *Studiengesellschaft Kohle, m.b.H.* v. *Shell Oil Co.*, 112 F.3d 1561, 1567 (Fed. Cir.), *cert. denied*, 522 U.S. 996 (1997). It has acknowledged that "[i]n several instances, this court has declined to apply the *Lear* doctrine." *Gen-Probe*, 359 F.3d at 1381. See also, *e.g.*, *Diamond Scientific Co.* v. *Ambico, Inc.*, 848 F.2d 1220, 1224-25 (Fed. Cir.) (*Lear* does not bar assignor estoppel), *id.* at 1228 (concurring opinion) (*Lear* rests on "outmoded theory" that "disserves the national interest"), *pet'n for cert. dismissed*, 487 U.S. 1265 (1988); *Foster* v. *Hallco Mfg. Co.*, 947 F.2d 469, 476 (Fed. Cir. 1991) ("[t]he Supreme Court in *Lear* did not consider the policy concerns" affecting a consent decree); *Flex-Foot*, 238 F.3d at 1368 ("this court has in the past distinguished a number of other cases from *Lear*"). But whether or not it agrees with this Court, the Federal Circuit is not at liberty to "ignore[] the guidance" of decisions of this Court. *Festo Corp.* v. *Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 739 (2002).

Now the Federal Circuit has invoked Article III to eliminate *Lear* itself, and effectively to revive licensee estoppel except for those licensees willing to commit breach of contract with all the accompanying risks as a precondition to challenging a patent. Unable to overturn *Lear* frontally under the patent laws, the Federal Circuit has adopted a constitutional holding that serves a policy exactly opposite to *Lear*—explaining that challenges like petitioner's would produce "undesirable results," *Gen-Probe*, 359 F.3d at 1382, "inequity," P.C.A. 7a. Already the present case has been recognized as holding that a licensee paying royalties "is estopped to challenge the validity of the patents in suit." *Advanced Card Technologies LLC* v. *Versatile Card Technology, Inc.*, 410 F. Supp. 2d 158, 161 (S.D.N.Y. 2006). And even if a patent license in spite of *Lear* could block a claim of invalidity or non-infringement, that still would be only a defense for the licensor, not a jurisdictional defect. "[A]bsence of a valid . . . cause of action does not implicate subject-matter jurisdiction." *Steel Co.* v. *Citizens for a Better Environment*, 523 U.S. 83, 89 (1998).

## III. ARTICLE III SHOULD NOT BE REINTERPRETED TO FREEZE FEDERAL PATENT POLICY.

The decision under review would reinterpret Article III of the Constitution, as implemented in the Declaratory Judgment Act. Even if the Federal Circuit were authorized to adopt its own patent policy contrary to *Lear*, there certainly was no basis or authority for that court to turn its view of desirable patent policy into an Article III holding. Most immediately, the present decision would disrupt a basic tenet of federal patent policy—encouragement of challenges to patent validity—and then elevate that revision to a constitutional ruling, beyond Congress's power to correct. *Cf. Seminole Tribe* v. *Florida*, 517 U.S. 44, 63 (1996) (for constitutional decisions "correction through legislative action is practically impossible"), quoting *Burnet* v. *Coronado Oil & Gas Co.*,

285 U.S. 393, 407 (1932) (Brandeis, J., dissenting). More broadly, the decision would excise from the Declaratory Judgment Act the heart of what Congress enacted, and call into question prior decisions of this Court.

### A. As a Constitutional Holding, the Decision Is Unsound and Disruptive.

Since its enactment in 1934 the declaratory judgment remedy has been a valuable resource in federal litigation to resolve a wide range of controversies, from commercial contracts to civil rights cases to insurance-coverage disputes, and its utility and role are well-recognized, "to enable parties to adjudicate their disputes before either suffers great damage." *Starter Corp.* v. *Converse, Inc.*, 84 F.3d 592, 596 (2d Cir. 1996) (declaratory "actions are particularly useful in resolving trademark disputes"); *Allstate Ins. Co.* v. *Green*, 825 F.2d 1061, 1064 (6th Cir. 1987) ("an extremely useful procedural device for adjudicating disputes concerning insurance"); see also, *e.g.*, *Hamlin Inc.* v. *Hartford Accident & Indem. Co.*, 86 F.3d 93, 94 (7th Cir. 1996) (Posner, C.J.) (insurance companies "often seek a declaratory judgment of noncoverage" in order "to avoid liability for breach"); *Whetstone Candy Co.* v. *Kraft Foods, Inc.*, 351 F.3d 1067, 1072 (11th Cir. 2003) (settlement agreement). To hold that Article III requires a party as a prerequisite to a declaratory judgment to perform the very act of which it wishes to ascertain the legality, would upset the law in many contexts beyond patents.

In so doing it would also disrupt the expectations of both patent licensees and licensors. Heretofore there has been no constitutional barrier to licensees' challenging patents while paying royalties under protest. The Federal Circuit soon after its creation in 1982 confirmed that established view. In *C.R. Bard, Inc.* v. *Schwartz*, 716 F.2d 874 (Fed. Cir. 1983)—which

the District Court here noted was controlling until *Gen-Probe*, see P.C.A. 24a—the Federal Circuit held:

> "We reject the blanket approach . . . that there can never be an apprehension of a federal infringement suit and thus no controversy when a license is still in effect."

716 F.2d at 880. That has been the law relied on by the district courts. *E.g.*, *Grid Systems Corp.* v. *Texas Instruments, Inc.*, 771 F. Supp. 1033, 1042 (N.D. Cal. 1991) (citing *C.R. Bard*); *Research Inst. for Med. Chemistry, Inc.* v. *Wisconsin Alumni Res. Found., Inc.*, 647 F. Supp. 761, 767 n.5 (W.D. Wis. 1986) (same). The district court that was reversed in *Gen-Probe* had thought it "settled law that an effective license between the parties does not preclude federal question jurisdiction over a licensee's declaratory judgment action."[16] Another district court likewise had held that "[a]lthough the parties are under license, there is a clear and concrete dispute between them about whether Synagis® infringes," but then overruled itself after *Gen-Probe*. *MedImmune, Inc.* v. *Centocor, Inc.*, 271 F. Supp. 2d 762, 768 (D. Md. 2003), *overruled*, 2004 U.S. Dist. Lexis 28800 (D. Md. June 17, 2004), *aff'd*, 409 F.3d 1376 (Fed. Cir. 2005), *pet'n for cert. pending* (No. 05-656). In this case as well, such was the understanding of the sophisticated attorneys representing respondents, who until *Gen-Probe* suddenly appeared had not challenged the subject-matter jurisdiction of the District Court. J.A. 149, 183; p. 8, *supra*.

Patent applications now approach 300,000 per year, and lately have been increasing 10% annually. See FTC Report, Exec. Sum. at 9. The number of patents tested in court is relatively small, and likely to remain so. Most patent licenses now in effect were negotiated and entered on the assumption that the pre-*Gen-Probe* understanding of the Declaratory

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[16] *Gen-Probe Inc.* v. *Vysis, Inc.*, No. 99-CV-2668, at 10 (S.D. Cal., Mar. 12, 2002), reprinted in Pet. Cert. in *Gen-Probe*, No. 04-260 (2004), at 25a.

Judgment Act, allowing declaratory suits by licensees, applied. "[C]ourts must be cautious before adopting changes that disrupt the settled expectations of the inventing community." *Festo*, 535 U.S. at 739.

### B. As Patent Policy, the Decision Is Unsound and Unauthorized.

Constitutional rules of general application concerning federal jurisdiction, like Article III's "Case" or "Controversy" requirement, should not be reconstructed to fit a patent policy. Even if that were permissible, the policy chosen by the Federal Circuit is not consistent with this Court's past interpretations of the patent laws. Although this Court repeatedly has emphasized that federal patent policy favors judicial testing of whether patents are valid, pp. 34-37, *supra*, the Federal Circuit instead has created a new, constitutionally entrenched, obstacle. And that Article III barrier would be erected at a time when commentators observe that the number of overbroad and invalid patents has grown far beyond the ability and resources of the PTO to control, and when practical inhibitions to such suits already are formidable.

#### 1. *Declaratory Actions by Licensees Do Not Unfairly Disadvantage Licensors.*

The Federal Circuit denounced "the inequity when the patent owner, having contracted away its right to sue, is in continuing risk of attack on the patent whenever the licensee chooses." P.C.A. 7a. It called this "undesirable." *Gen-Probe*, 359 F.3d at 1382.

However, this Court in *Lear* announced exactly the opposite judgment. Emphasizing "the demands of the public interest," 395 U.S. at 670, this Court addressed head-on and rejected "[t]he theory . . . that a licensee should not be permitted to enjoy the benefit afforded by the agreement while simultaneously urging that the patent which forms the basis of the agreement is void." *Id.* at 656.

> "[I]t does not seem to us to be unfair to require a patentee to defend the Patent Office's judgment when his licensee places the question in issue, especially since the licensor's case is buttressed by the presumption of validity which attaches to his patent."

*Id.* at 670. "[T]he seeming inequity of allowing a licensee to keep his license while he attacks the validity of the licensor's patent is outweighed by the public interest in placing no impediment in the way of those in the best position to contest the validity of the underlying patent." *Warner-Jenkinson Co. v. Allied Chem. Corp.*, 567 F.2d 184, 188 (2d Cir. 1977); see also *American Sterilizer Co.* v. *Sybron Corp.*, 526 F.2d 542, 546-47 (3d Cir. 1975) ("We read the Supreme Court's opinion in *Lear* as resolving the competing equities between the licensee and the licensor in favor of the licensee.").

The Federal Circuit's policy argument forgets this Court's conclusion that

> "the equities of the licensor do not weigh very heavily when they are balanced against the important public interest in permitting full and free competition in the use of ideas which are in reality a part of the public domain."

*Lear*, 395 U.S. at 670. "A patent by its very nature is affected with a public interest" that is "recognized by the Constitution." *Precision Instrument*, 324 U.S. at 816. The public is a silent party in all patent-validity litigation.

Moreover, there is no rule that a patentee may not seek a declaratory judgment; enjoying the presumption of validity, however, few have reason to do so. See *Talbot* v. *Quaker State Ref. Co.*, 104 F.2d 967, 968 (3d Cir. 1939); see also *Lang* v. *Pacific Marine & Supply Co.*, 895 F.2d 761, 764 (Fed. Cir. 1990) ("no reason why a patentee should be unable to seek a declaration of infringement against a future infringer"); *Metabolite Labs., Inc.* v. *Laboratory Corp. of America Holdings*, 370 F.3d 1354, 1369 (Fed. Cir. 2004) (same), *cert. granted on another point*, 126 S. Ct. 601 (2005)

(No. 04-607); 10B C. WRIGHT, *et al.*, FEDERAL PRACTICE & PROCEDURE § 2761 at 572 (1998).

It is quite correct that licensor and licensee do not stand on equal footing—but the advantages are on the side of the licensor. "[P]atentees are heavily favored as a class of litigants by the patent statute." *Blonder-Tongue*, 402 U.S. at 335. Patents—and every claim within those patents—are statutorily *presumed* valid and "[t]he burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity." 35 U.S.C. § 282. Further, this presumption of validity cannot be overcome except by "clear and convincing evidence." *State Contracting & Engineering Corp.* v. *Condotte America, Inc.*, 346 F.3d 1057, 1067 (Fed. Cir. 2003). Given the powerful presumption of validity, there is little need for a licensor to obtain further confirmation of its patent's validity outside an infringement action.

The Court of Appeals also opined that "[a]llowing this action to proceed would . . . discourage patentees from granting licenses." *Gen-Probe*, 359 F.3d at 1382. But that speculation is unsupported. There is no evidence that patent-licensing abated after *Lear*, nor that such would occur if jurisdictional law returns to the pre-*Gen-Probe* norm. Nor is the assumption logical. Patentees grant licenses to generate royalties. Their financial incentive to do so is not altered by whether licensees can sue without breach. If a patentee preferred instead not to license, but rather to use its patent to prevent competition, it would not have licensed in the first place. Removing the licensee's ability to challenge validity in a declaratory action would simply add to the economic power of the patent.

Also, any attempt to weigh fairness would consider that patent licenses often are entered under economic constraint, and sometimes without full information. "[C]ompanies and individuals must constantly fear that their research and product development may come to naught, because someone is going to assert an as-yet unknown or untested patent

against them." A. JAFFE & J. LERNER, INNOVATION AND ITS DISCONTENTS 172 (2004). This "often leads either to abandonment of the allegedly infringing technology, or to an agreement to pay possibly unnecessary royalties." *Id.* Sometimes, too, as here, a patentee's potentially invalid claims may not be known when the license is entered. The Cabilly II application claimed an invention date of 1983, was not filed until 1988, was vastly broadened in 1989, provoking a lengthy interference proceeding, and was not issued as a patent and its claims revealed until its issuance (to the consternation of the PTO Board, p. 5, *supra*) in 2001—four years after MedImmune's license.

Finally, if in a particular case declaratory relief really would involve unfairness, the Act itself provides a solution. Declaratory relief, like an injunction, is discretionary. *Wilton* v. *Seven Falls Co.*, 515 U.S. 277, 286-88 (1995); *Cardinal Chemical*, 508 U.S. at 95 n.17; *Brillhart* v. *Excess Ins. Co.*, 316 U.S. 491, 494 (1942). Discretion looks, for example, to "whether the judgment will serve a useful purpose in clarifying or settling the legal issues involved" and "finalize the controversy and offer relief from uncertainty." *Duane Reade, Inc.* v. *St. Paul Fire & Marine Ins. Co.*, 411 F.3d 384, 389 (2d Cir. 2005). The Federal Circuit, however, would deny district courts the jurisdiction to exercise that discretion. Accordingly, here the District Court obediently dismissed for lack of subject-matter jurisdiction, with no opportunity "to exercise *any discretion at all*." *Cardinal Chemical*, 508 U.S. at 103 (Scalia, J., concurring in part) (emphasis in original).

### 2. *The Federal Circuit's Decision Would Add Another Disincentive to Patent Challenges.*

To establish a patent's invalidity is likely to demand "great effort and expense." *Cardinal Chemical*, 508 U.S. at 99, quoting *Morton Int'l, Inc.* v. *Cardinal Chem. Co.*, 967 F.2d 1571, 1577 (Fed. Cir. 1992) (Nies, J., dissenting from denial of rehearing *en banc*), *vacated*, 508 U.S. 83 (1993). It has

been estimated that to challenge a patent can cost in legal fees $5-7 million. See FTC Report, Ex. Sum. at 6, ch. 3 at 22; see also Lerner, *Patenting in the Shadow of Competitors*, 38 J.L. & ECON. 463, 470 (1995). A challenger faces also the statutory presumption of validity, 35 U.S.C. § 282, which lets a patentee "easily put the alleged infringer to his expensive proof," so that "prospective defendants will often decide that paying royalties under a license or other settlement is preferable to the costly burden of challenging the patent." *Cardinal Chemical*, 508 U.S. at 101 n.24, quoting *Blonder-Tongue*, 402 U.S. at 338.

Licensees often enter licenses reluctantly. Small, start-up companies, particularly in the pharmaceutical and biotechnology industries, may agree to be bound by licenses for patents of uncertain scope and validity because the licensee may be unable to afford the high cost of patent litigation. As this Court observed in *Lear*, "by accepting a license and paying royalties for a time, the licensee may have avoided the necessity of defending an expensive infringement action during the period when he may be least able to afford one." 395 U.S. at 669. Small start-up companies and even larger ones may, like MedImmune, depend on a single product for most of their revenue.[17] Quite understandably, such entrepreneurs may find it imprudent to forgo a license and risk an injunction of their principal product, which could effectively put them out of business. MedImmune, of course, was acutely aware of the risks of defying Genentech's demand, by stopping payments in a bet-the-company legal judgment jeopardizing its principal product, instead of resolving the matter by declaratory adjudication. J.A. 389, 393.

Licensees may not be sure what a license ultimately will purport to include. Here MedImmune agreed to the license from Genentech in 1997. The Cabilly II patent was not

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[17] More than 80% of MedImmune's revenues from 1999 to 2003 depended on Synagis®, J.A. 387, and the same is true since then.

issued and its claims disclosed until late in 2001. Genentech's demand for royalty payments followed in a matter of days. J.A. 414. Given the high cost of litigation to test the validity of a patent, a small company is unlikely to undertake such a challenge unless and until the product is successful enough to generate large revenues, carrying a correspondingly increasing burden of royalty payments. See FTC Report, ch. 3 at 29 (observations that "litigation is too expensive and time-consuming for small biotechnology companies"). At the time of the 1997 license, Synagis® had not been approved by the FDA. By the time MedImmune sought a declaratory judgment, royalties demanded had risen to millions of dollars per year.

Licensees often agree to a single license for several patents and products together, and with a provision that failure to pay any royalty due is a material breach of the entire contract. The prudent licensee very likely will be unwilling to lose its license to all the patents or products, if that is the consequence of challenging a demand based on one patent it believes invalid or not infringed. The licensee's dilemma is heightened in a case like the present one, in which not all the licensed claims are known at the time of licensing, and later there appears a broad "continuation" patent, the claims of which the licensee does not learn until years after agreeing to the license.

### 3. *Preventing Licensee Patent Challenges Would Disserve a Rapidly Evolving Technological Economy.*

Presciently this Court warned in *Lear* that to disallow licensee challenges to patent validity would have an effect "particularly severe in the many scientific fields in which invention is proceeding at a rapid rate." 395 U.S. at 673. A "zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention . . . ." *Markman* v. *Westview Instruments, Inc.*, 517 U.S. 370, 390 (1996), quoting *United Carbon*

*Co.* v. *Binney & Smith Co.*, 317 U.S. 228, 236 (1942), and citing *Merrill* v. *Yeomans*, 94 U.S. 568, 573 (1877). That is certainly true for biotechnology, and also for active fields like electronic information, communications, medicine and others of highest innovation. "Firms in the biotechnology industry reported that they avoid infringing even questionable patents and therefore refrain from entering or continuing with a particular field of research." FTC Report, ch. 3 at 21. Also, "invalid patents" are "hampering pharmaceutical innovation." Derzko, *The Impact of Recent Reforms*, 45 IDEA: J.L. & TECH. 165, 265 (2005). "[T]he pattern of costly litigation—or payments to forestall litigation—are leading to reductions or distortions in innovative investments, particularly for small firms." Lerner at 471.

Burdens on challenging patents are less appropriate today than ever. The increasingly ineffective scrutiny applied in issuing patents has been widely criticized. *E.g.*, A. JAFFE & J. LERNER at 34 (PTO is "so overtaxed, and its incentives have become so skewed towards granting patents"); FTC Report, Exec. Sum. at 8-10, ch. 3 at 19, ch. 5 at 5-8. By various estimates the PTO grants 74% to 98% of all patent applications, which now approach 300,000 per year. *Id.*, Exec. Sum. at 9, ch. 5 at 6; NATIONAL RESEARCH COUNCIL, A PATENT SYSTEM FOR THE 21ST CENTURY 52-55 (2004). "[T]he ultimate granting of some patent from each original application has become almost a sure thing." A. JAFFE & J. LERNER at 171. But when validity is challenged and litigated to final judgment, about 45% of patents are held invalid. FTC Report, ch. 5 at 6. Such "an indiscriminate creation of exclusive privileges tends rather to obstruct than to stimulate invention." *Atlantic Works* v. *Brady*, 107 U.S. 192, 200 (1883). See also *Lear*, 395 U.S. at 674 n.19 ("public's interest in the elimination of specious patents").

This Court has pointed out that patents are granted "in an *ex parte* proceeding, without the aid of the arguments which could be advanced by parties interested in proving patent invalidity." *Lear*, 395 U.S. at 670.[18] The public's interest is not only to reward useful innovation, but also to ensure that unpatentable ideas remain in the public domain, encouraging innovation, investment, competition, and lower costs to consumers. It is also to prevent higher prices of medicines and other commodities resulting from royalties paid to holders of invalid patents. FTC Report, Exec. Sum. at 6-7.

"Licensees may often be the only individuals with enough economic incentive to challenge the patentability of an inventor's discovery." *Lear*, 395 U.S. at 670. If licensees are prevented from testing validity without giving up their licenses and risking ruin, there will be fewer challengers to step forward to undertake that role.

### C. Patent Policy Should Be Revised by Congress Legislating Under Article I, Not by Courts Reinterpreting Article III.

If changes in the legal relationships of licensors and licensees of patents are to be adopted, such adjustments are constitutionally assigned to Congress by Article I. See

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[18] The narrow and limited procedure of patent reexamination under 35 U.S.C. §§ 301-302 is *ex parte* and considers only prior printed publications and patents. Reexamination is not available for other fundamental violations raised here, such as lack of enablement or written description, fraud on the Patent Office, prior acts evidencing invention by another, non-infringement, etc. The PTO has granted two requests for reexamination of the Cabilly II patent under § 302, one by petitioner. A preliminary ruling has held the Cabilly II patent invalid for obviousness-type double-patenting. (Reexamination under 35 U.S.C. § 311, not pertinent here, is not *ex parte*, but otherwise suffers from the same limitations, plus a number of others.) See generally A. JAFFE & J. LERNER at 186-88; FTC Report, ch. 3 at 21 (reexamination mechanisms "are generally inadequate").

*Diamond* v. *Chakrabarty*, 447 U.S. 303, 317 (1980) (in addressing scope of patentable subject matter, "the contentions now pressed on us should be addressed to the political branches of the Government"); *cf. Hartford Underwriters Ins. Co.* v. *Union Planters Bank, N.A.*, 530 U.S. 1, 13-14 (2000) (bankruptcy policy); *Turner Broadcasting System, Inc.* v. *FCC*, 520 U.S. 180, 224 (1997) (communications policy). Congress, for its part, pays active and frequent attention to adjusting patent provisions: "our patent and copyright statutes have been amended repeatedly." *Sony Corp.* v. *Universal City Studios, Inc.*, 464 U.S. 417, 429 (1984).[19] Revising intellectual-property policy falls "inside the domain the Constitution assigns to the First Branch." *Eldred* v. *Ashcroft*, 537 U.S. 186, 222 (2003). So, for that matter, does revising the statutory jurisdiction of the federal courts within Article III. *Sheldon* v. *Sill*, 8 How. 441, 449 (1850). "Congress can legislate" on those subjects "any time it chooses." *Warner-Jenkinson Co.* v. *Hilton Davis Chem. Co.*, 520 U.S. 17, 28 (1997).

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[19] "[T]he Patent Act was amended, revised or codified some 50 times between 1790 and 1950," *Graham* v. *John Deere Co.*, 383 U.S. 1, 10 (1966), and in recent years the pace of amendment has not slackened. See 118 Stat. 3596 (2004); 117 Stat. 2066 (2003); 116 Stat. 1758 (2002); 114 Stat. 1742 (2000); 113 Stat. 1501 (1999); 112 Stat. 2780 (1998); 109 Stat. 351 (1995); 108 Stat. 4809 (1994); 107 Stat. 2057 (1993).

## CONCLUSION

For the reasons stated, the judgment of the Court of Appeals should be reversed.

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# ADDENDUM

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## CONSTITUTIONAL AND STATUTORY PROVISIONS AND RULE

Article III, § 2, of the Constitution of the United States provides in part:

> "The judicial Power shall extend to all Cases, in Law and Equity, arising under this Constitution, the Laws of the United States . . . .

Title 28 U.S.C. § 1331 provides:

> The district courts shall have original jurisdiction of all civil actions arising under the Constitution, laws, or treaties of the United States.

Title 28 U.S.C. § 1338(a) provides:

> The district courts shall have original jurisdiction of any civil action arising under any act of Congress relating to patents, plant variety protection, copyrights and trademarks. Such jurisdiction shall be exclusive of the courts of the states in patent, plant variety protection and copyright cases.

Title 28 U.S.C. § 2201(a) provides:

> In a case of actual controversy within its jurisdiction, except with respect to Federal taxes other than actions brought under section 7428 of the Internal Revenue Code of 1986, a proceeding under section 505 or 1146 of title 11, or in any civil action involving an antidumping or countervailing duty proceeding regarding a class or kind of merchandise of a free trade area country (as defined in section 516A(f)(10) of the Tariff Act of 1930), as determined by the administering authority, any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested party seeking such decla-

ration, whether or not further relief is or could be sought. Any such declaration shall have the force and effect of a final judgment or decree and shall be reviewable as such.

Title 28 U.S.C. § 2202 provides:

Further relief

Further necessary or proper relief based on a declaratory judgment or decree may be granted, after reasonable notice and hearing, against any adverse party whose rights have been determined by such judgment.

Title 35 U.S.C. § 135(a) provides:

Interferences

(a) Whenever an application is made for a patent which, in the opinion of the Director, would interfere with any pending application, or with any unexpired patent, an interference may be declared and the Director shall give notice of such declaration to the applicants, or applicant and patentee, as the case may be. The Board of Patent Appeals and Interferences shall determine questions of priority of the inventions and may determine questions of patentability. Any final decision, if adverse to the claim of an applicant, shall constitute the final refusal by the Patent and Trademark Office of the claims involved, and the Director may issue a patent to the applicant who is adjudged the prior inventor. A final judgment adverse to a patentee from which no appeal or other review has been or can be taken or had shall constitute cancellation of the claims involved in the patent, and notice of such cancellation shall be endorsed on copies of the patent distributed after such cancellation by the Patent and Trademark Office.

Title 35 U.S.C. § 282 provides in part:

> Presumption of validity; defenses
>
> A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. Notwithstanding the preceding sentence, if a claim to a composition of matter is held invalid and that claim was the basis of a determination of nonobviousness under section 103(b)(1), the process shall no longer be considered nonobvious solely on the basis of section 103(b)(1). The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.
>
> The following shall be defenses in any action involving the validity or infringement of a patent and shall be pleaded:
>
> (1) Noninfringement, absence of liability for infringement or unenforceability,
>
> (2) Invalidity of the patent or any claim in suit on any ground specified in part II of this title as a condition for patentability,
>
> (3) Invalidity of the patent or any claim in suit for failure to comply with any requirement of sections 112 or 251 of this title,
>
> (4) Any other fact or act made a defense by this title. . . .

Title 35 U.S.C. § 283 provides:

> Injunction
>
> The several courts having jurisdiction of cases under this title may grant injunctions in accordance with the

principles of equity to prevent the violation of any right secured by patent, on such terms as the court deems reasonable.

Title 35 U.S.C. § 284 provides:

Damages

Upon finding for the claimant the court shall award the claimant damages adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use made of the invention by the infringer, together with interest and costs as fixed by the court.

When the damages are not found by a jury, the court shall assess them. In either event the court may increase the damages up to three times the amount found or assessed. Increased damages under this paragraph shall not apply to provisional rights under section 154(d) of this title.

The court may receive expert testimony as an aid to the determination of damages or of what royalty would be reasonable under the circumstances.

Title 35 U.S.C. § 285 provides:

Attorneys Fees

The court in exceptional cases may award reasonable attorney fees to the prevailing party.

Rule 57, Federal Rules of Civil Procedure, provides:

Declaratory Judgments.

The procedure for obtaining a declaratory judgment pursuant to Title 28, U.S.C., § 2201, shall be in accordance with these rules, and the right to trial by jury may be demanded under the circumstances and in the manner provided in Rules 38 and 39. The existence of

another adequate remedy does not preclude a judgment for declaratory relief in cases where it is appropriate. The court may order a speedy hearing of an action for a declaratory judgment and may advance it on the calendar.

188d

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No. 05-608

Supreme Court, U.S.
FILED
JUL 24 2006

IN THE
# Supreme Court of the United States

MEDIMMUNE, INC.,
*Petitioner,*
v.
GENENTECH, INC. and CITY OF HOPE
*Respondents.*

On Writ of Certiorari
to the United States Court of Appeals
for the Federal Circuit

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## QUESTION PRESENTED

When a patent licensee maintains its good standing under its license in order to preserve its immunity from suit by the patent owner, may the licensee nonetheless obtain judicial advice regarding the validity and enforceability of the licensed patent to help it decide whether or not to repudiate its contractual royalty obligations, while at the same time holding the patent owner to its side of the bargain?

## LIST OF PARTIES

Petitioner MedImmune, Inc. was the only plaintiff and appellant in the courts below. City of Hope, Genentech, Inc., and Celltech R&D, Ltd. were the defendants-appellees. City of Hope and Genentech are the only Respondents in this Court, because Petitioner did not seek review of the Court of Appeals' ruling concerning Celltech.

## RULE 29.6 DISCLOSURE

Respondent City of Hope is a California non-profit public benefit biomedical research, treatment and educational institution. City of Hope has no parent company. No entity owns stock in City of Hope.

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## STATUTES INVOLVED

Relevant constitutional and statutory provisions are set out in the Statutory Addendum to this brief.

## STATEMENT OF THE CASE

MedImmune entered into a patent license in which it agreed to pay royalties in exchange for immunity from being sued for infringement. Then MedImmune itself sued in order to escape its royalty obligations under the license, but continued to claim the benefit of the license for itself as a shield against an infringement suit. The law does not permit patent licensees to exploit their licenses in this way. MedImmune's action is barred by Article III because its continued maintenance of the license as a shield against suit prevents a ripe and actionable controversy from arising. In addition, under long-standing rules of equity – which govern the exercise of declaratory judgment jurisdiction – a licensee may not attack the validity of a patent unless it first surrenders the benefits of the license by repudiation, thereby placing the parties on a level playing field.

### A. Factual Background

***The Cabilly II Patent.*** Respondent City of Hope is a California-based nonprofit organization known for its National Cancer Institute-designated Comprehensive Cancer Center and ground-breaking biomedical research. City of Hope employs more than 300 physicians and scientists who work to find the causes of and cures for cancer and other life-threatening diseases, including diabetes and HIV/AIDS. In the early 1980s, City of Hope and respondent Genentech, Inc. worked collaboratively on research developing recombinant DNA technology. J.A. 109 ¶21, 417, 485, 509. The collaboration resulted in several pioneering technologies for the production of immunoglobulins and engineered immunoglobulin chains, including techniques that are now

used in the biotechnology industry to engineer and produce life-saving therapeutic antibodies.

City of Hope and Genentech sought patent protection for these breakthroughs. On April 8, 1983, Genentech filed a patent application with the Patent and Trademark Office ("PTO") on behalf of itself and City of Hope (the "Cabilly I Application"). J.A. 109 ¶ 21, 485. The application disclosed at least two sets of inventions: one relating to engineering techniques to produce chimeric heavy or light immunoglobulin chains ("chimeric chains"); the other relating to techniques for coexpressing heavy and light immunoglobulin chains in the same cell to produce assembled immunoglobulins ("coexpression").

On November 14, 1984, another company, Celltech R&D Ltd., filed an application with the PTO relating to the coexpression technology. J.A. 276-80, 459. Celltech's application claimed priority based on a British patent application filed just two weeks before the Cabilly I Application, on March 25, 1983. J.A. 276-80, 459. Under rules then in effect, Celltech's application was confidential and not disclosed to Genentech or City of Hope.

On June 10, 1988, Genentech filed a new application as a "continuation" of the Cabilly I Application, *i.e.*, one based on the same disclosure in Cabilly I but adding new claims (the "Cabilly II Application"). *See* J.A. 47 ¶ 23. As a continuation, the Cabilly II Application is entitled to the same priority date as Cabilly I. 35 U.S.C. § 120.

On March 28, 1989, the PTO granted the Cabilly I Application and issued U.S. Patent No. 4,816,567, which covers the chimeric chain technology (the "Cabilly I Patent"). J.A. 485. On the same day, the PTO also granted Celltech's application and issued U.S. Patent No. 4,816,397 (the "Boss Patent"). J.A. 459.

Genentech recognized that the Boss Patent's claims covered the coexpression technology disclosed but not claimed in the earlier-filed Cabilly I Application. Accordingly, to provoke an "interference" proceeding in which the PTO and the courts could determine which company could properly claim inventorship, Genentech amended the claims of its pending Cabilly II Application to match the claims of the issued Boss Patent. J.A. 278; *see also* J.A. 345 (copying claims is "the permitted and standard procedure for provoking an interference").

The PTO's Board of Patent Appeals and Interferences ("BPAI") then declared an interference between the Boss Patent and the Cabilly II Application in order to determine which party had priority to the invention, *i.e.*, which party's action triggering patent protection occurred first. 35 U.S.C. § 135(a); *Cabilly v. Boss*, 55 U.S.P.Q.2d 1238 (Bd. Pat. App. & Interf. 1998); J.A. 109. In general, the first party to conceive of an invention and reduce it to practice is entitled to priority – not the first party to file a patent application. 35 U.S.C. §102(g)(2); *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 61 (1998). Genentech and Celltech diligently litigated that issue, but for unexplained reasons the BPAI did not issue its decision for more than six years after the parties submitted their papers, and more than four years after oral argument. The BPAI found that Genentech had not met its evidentiary burden of establishing earlier conception and reduction to practice. *Cabilly*, 55 U.S.P.Q.2d at 1256.

Genentech challenged the BPAI's ruling by filing a civil interference action against Celltech in federal court. *See* 35 U.S.C. § 146. Parties in such a case may introduce evidence not submitted to the BPAI. *Id.* While the case was pending, Genentech located a draft application for Cabilly I from February 1983 – a month before Celltech's British application. J.A. 281-323; *see* J.A. 272-73 ¶¶ 4-5, 325-29. The draft application is a lengthy and detailed description of

the inventions and showed that City of Hope and Genentech had priority over Celltech. J.A. 281-323.

Relying on this new and persuasive evidence, Genentech moved for summary adjudication, J.A. 273 ¶ 9, but the court strongly encouraged the parties to settle the matter with the help of a mediator, J.A. 331-33; *see also* Pet. App. 3a. In the resulting settlement, which the district court approved as a consent judgment, Celltech conceded that City of Hope's and Genentech's application had priority over the Boss Patent. J.A. 345-46; *see* J.A. 274 ¶¶ 12-13, 345-46 ¶¶ 9-10. The PTO then independently reviewed the pending claims of the Cabilly II Application, concluding that they were valid.[1] Thus, on December 18, 2001, after suffering years of administrative and litigation delay, City of Hope and Genentech finally obtained U.S. Patent No. 6,331,415B1 (the "Cabilly II Patent"). J.A. 509-50; *see also* J.A. 551 (certificate of correction listing City of Hope as co-assignee). Under applicable law, Cabilly II's term runs for 17 years from issuance. *See* 35 U.S.C. § 154 (1994).

Genentech uses Cabilly II's technologies in five of its products, including treatments for breast and colorectal cancer. City of Hope uses revenue from the licensing of the

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[1] Although the district court ordered the PTO to cancel the Boss Patent and issue Cabilly II, the PTO did not carry out these parts of the order. The PTO gave conclusive effect to the court's judgment *only* on the issue of Cabilly II's priority over Boss. The PTO independently ensured that Cabilly II satisfied all other requirements for patentability. J.A. 347-48; *Cabilly v. Boss*, 60 U.S.P.Q.2d 1752 (Bd. Pat. App. & Interf. 2001).

The United States also asserts – without citation – that the parties' settlement gave Celltech the right to share in all royalties Genentech receives on the Cabilly II Patent. U.S. Br. 4-5 n.3. That is wrong. Celltech only received a share of the royalties for a limited period of time (that has now ended), and its share was substantially lower than what it would have received under its Boss Patent but for the settlement. *See* Fed. Cir. J.A. 1713-44.

patent to support its nonprofit basic and biomedical research programs.

***MedImmune's License.*** Petitioner MedImmune, Inc. produces its product Synagis using the method disclosed in both Cabilly patents and claimed in Cabilly II. *Compare* MedImmune Br. 2-3 (describing how Synagis is made), *with id.* at 4-5 (describing claims of Cabilly II in same terms).

While the interference between Genentech and Celltech was pending, MedImmune sought and received licenses from both companies to ensure that Synagis would not infringe regardless of which company had priority. *See* J.A. 134 ¶ 122. On June 4, 1997, MedImmune obtained its license from Genentech (acting on behalf of itself and City of Hope) under the Cabilly I Patent and "any patent issuing based on" the Cabilly II Application. J.A. 399. The license thus expressly contemplated that Genentech might receive a patent within the scope of Cabilly II. The entire reason MedImmune obtained the license for "any patent" based on the Cabilly II Application was to insure that it could not be sued for infringement if a patent issued on that application.

In addition to authorizing MedImmune to use the methods covered by the patents, the license grants MedImmune "co-exclusive" rights, in that Genentech could grant no more than four additional licenses for the same field and territory. J.A. 401. By taking the license at an early stage, MedImmune also locked in a favorable royalty rate reflecting at least two contingencies: MedImmune's product Synagis was still in development and had not been approved by the FDA, *see* Fed. Cir. J.A. 3311 (initial license fee is higher for products further in development), and Genentech and City of Hope had not received the Cabilly II Patent. MedImmune also obtained a most-favored licensee guarantee and the right to terminate the license for any reason with six months' notice. J.A. 405, 409.

In the license, MedImmune agreed to pay royalties when it practices claims of the licensed patents "which have neither expired nor been held invalid by a court or other body of competent jurisdiction from which no appeal has been or may be taken." J.A. 399, 406.[2] The background law against which the parties contracted also gives MedImmune an unconditional right to repudiate the license, stop paying royalties, and then assert patent invalidity as a defense in a lawsuit for post-repudiation damages. *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969). However, under Federal Circuit law in effect at the time the license was executed, "a licensee . . . cannot invoke the protection of the *Lear* doctrine until it (i) actually ceases payment of royalties, and (ii) provides notice to the licensor that the reason for ceasing payment of royalties is because it has deemed the relevant claims to be invalid." *Studiengesellschaft Kohle, m.b.H. v. Shell Oil Co.*, 112 F.3d 1561, 1568 (Fed. Cir. 1997). Nothing in the license purports to contract around that rule to allow MedImmune to challenge the patent while claiming the benefit of the license.

***The Parties' Dealings Under the License.*** In 1999, Genentech sought royalties from MedImmune for Synagis under the Cabilly I Patent. J.A. 414-15. MedImmune refused, asserting that Synagis fell outside the scope of Cabilly I. J.A. 416. Genentech accepted that response and took no action against MedImmune. MedImmune never paid royalties under Cabilly I, which is not at issue here. J.A. 388.

On January 7, 2002, after the Cabilly II Patent issued, Genentech sought royalties from MedImmune on sales of Synagis under Cabilly II. J.A. 419-20. In its response, dated February 13, 2002, MedImmune did not dispute that royalties

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[2] MedImmune truncates its quotation of this term of the license to create the false impression that the license contemplates that the patents' validity is an open question even in the absence of a final and unappealable judgment of invalidity. Pet'r Br. 4.

were due or raise any specific questions as to validity, enforceability, or infringement. It stated merely that "it would be helpful if you could please advise us as to your basis for believing that MedImmune's product would infringe any valid claim of the [Cabilly II] Patent such that royalties would be due." J.A. 421. The letter went on to request *additional* licenses under the Cabilly II Patent for other products MedImmune wanted to develop. J.A. 422.

Two weeks later, before Genentech responded, MedImmune commenced royalty payments. J.A. 426. A few days after that, MedImmune faxed a letter asserting that its payment was "under protest" – without indicating the nature or basis of the "protest." J.A. 426. Two weeks later, Genentech replied to MedImmune, explaining its understanding that Synagis falls within the scope of the Cabilly II Patent, but asking MedImmune (if it disagreed) to explain the process MedImmune uses to manufacture Synagis "so that we may reevaluate our position." J.A. 428. As this response shows, Genentech understood MedImmune's "protest" as relating to whether MedImmune uses the method claimed in Cabilly II in producing Synagis, just as MedImmune had earlier (successfully) contended that it did not use the method claimed in Cabilly I.

At no point did MedImmune state that it believed Cabilly II was invalid or unenforceable. Instead, MedImmune continued to press for additional licenses to cover more products it had in the pipeline. J.A. 431. MedImmune emphasized that "Genentech's licensing policy with respect to the [Cabilly II] patent has the potential to be a significant factor in MedImmune's research and development strategies." J.A. 431. In the subsequent negotiations for the additional licenses (*see* J.A. 433-35), MedImmune had the opportunity to raise arguments about validity, enforceability, or any other patent issue that could affect the royalty rate or other licensing terms. But MedImmune raised no such

issues, and it received licenses for seven more product lines in January 2003 – more than a year after Cabilly II issued and MedImmune became fully aware of the patent's claims and prosecution history. J.A. 108, 134, 437-453.

**B. Procedural History**

***District Court Proceedings.*** Less than three months after it had secured its position with its new licenses, MedImmune filed this lawsuit seeking, *inter alia*, declaratory judgments that the Cabilly II Patent is invalid and unenforceable. J.A. 1, 41.[3] At all times relevant to this case, however, MedImmune has sought to retain the benefits of its license for Synagis by continuing to pay royalties. J.A. 389. Yet it inflicted on City of Hope and Genentech the precise burden the license was intended to avoid – patent litigation.[4]

In its first responsive pleading, City of Hope asserted nonjusticiability defenses to these claims. J.A. 222 ¶¶ 8, 10. Initially, however, the district court proceedings focused on antitrust claims that MedImmune had asserted against Genentech and Celltech (but not City of Hope). *See* J.A. 141-46. After the district court dismissed the antitrust counts on the merits, J.A. 349-71, Genentech and City of Hope moved to dismiss MedImmune's declaratory claims as nonjusticiable. J.A. 382-83, 384. The court granted the motions under *Gen-Probe Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir. 2004). Pet. App. 21a-31a; J.A. 436.

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[3] As set forth more fully in Genentech's brief, MedImmune's complaint does not allege any basis for claiming that the production of Synagis is not covered by the license, *i.e.*, does not use the technique claimed in Cabilly II. Rather, MedImmune artfully pleads its purported contract and infringement claims to incorporate the patent validity and enforceability issues that are the focus of its complaint. *See* J.A. 115-30, 136-41.

[4] MedImmune has made this "license and sue" tactic its standard practice. *See, e.g., MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376, 1378 (Fed. Cir.), *petition for cert. filed*, 74 U.S.L.W. 3336 (U.S. Nov. 22, 2005) (No. 05-656).

***Federal Circuit Appeal.*** The Federal Circuit affirmed, concluding that MedImmune's declaratory claims do not present a justiciable controversy because "MedImmune is complying fully with the license terms and cannot be sued by the patentee[s]." Pet. App. 5a. The court rejected MedImmune's reliance on *Lear v. Adkins* because, in sharp contrast to that case, "MedImmune is paying the license royalties; and . . . Genentech has no ground on which to cancel the license or otherwise bring suit affecting the licensed subject matter." Pet. App. 5a. The court stressed "the inequity [that would result] when the patent owner, having contracted away its right to sue, is in continuing risk of attack on the patent whenever the licensee chooses – for example, if the product achieves commercial success – while the licensee can preserve its license and royalty rate if the attack fails. This imbalance distorts the equalizing principles that underlie the Declaratory Judgment Act." Pet. App. 7a. Given that "MedImmune avoided and continues to avoid" taking actions that would create a justiciable controversy, the Federal Circuit held that Article III's requirements had not been met. Pet. App. 8a.[5]

***Administrative Reexamination.*** The PTO is presently reexamining the Cabilly II Patent in two *ex parte* proceedings under 35 U.S.C. §§ 301-305. MedImmune anonymously initiated one of these proceedings after petitioning this Court for certiorari but before filing its reply at the certiorari stage. *See* Pet'r Br. 48 n.18. MedImmune did not disclose its pending reexamination request to the Court at that time. To date, the PTO has issued an initial office action rejecting the claims of Cabilly II. Such initial rejections are an ordinary part of the back-and-forth between the PTO and patentees, however, similar to the process on initial patent applications,

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[5] The court also affirmed dismissal of MedImmune's antitrust claims, Pet. App. 2a, and MedImmune did not seek review of that ruling in this Court.

and are not good indicators of the ultimate outcome.[6] In 88% of cases, a patent subject to *ex parte* reexamination survives in whole or part. *See* Wayne O. Stacy, *Reexamination Reality*, 66 Geo. Wash. L. Rev. 172, 182-83 (1997).

## SUMMARY OF ARGUMENT

1. Because MedImmune's license bars any suit by Genentech and City of Hope, and because MedImmune lacks any right of action for affirmative relief against Respondents, there is no ripe justiciable controversy here. Article III extends the federal judicial power to cases or controversies in law and equity – categories whose parameters are informed by the historical business of Anglo-American courts. The Declaratory Judgment Act ("DJA"), 28 U.S.C. § 2201 *et seq.*, did not expand that jurisdiction or create new substantive rights. It simply provided a new procedure for obtaining adjudication of controversies already within the courts' preexisting jurisdiction. Hence, there must already be a ripe controversy cognizable in law or equity for there to be a ripe controversy for declaratory relief.

Within these bounds, the declaratory procedure performs important functions. In a "mirror-image" declaratory suit, the DJA allows the party who would be the defendant in a conventional suit to take the initiative as plaintiff and sue for a declaration of nonliability – but only if the declaratory defendant presently has a ripe claim for conventional relief. Such a declaratory suit is simply the mirror image of a ripe conventional controversy. The DJA also allows the plaintiff in a conventional suit to seek declaratory relief in addition to,

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[6] *See Lear*, 395 U.S. at 658 (describing typical procedure of rejections by PTO and responses by applicant); 35 U.S.C. § 305 (extending initial examination procedures to reexamination); Patent & Trademark Off., Dep't of Commerce, *Manual of Patent Examining Procedure* § 706.02(b) (8th ed. 2005) (providing that PTO rejection can be overcome by argument for rejected claim or by amendment of claim).

or instead of, conventional relief. For example, in a suit for a declaration that a law is unconstitutional, there is a justiciable controversy because the plaintiff already has a ripe claim for an injunction under *Ex parte Young* and § 1983.

But this Court has *never* approved a declaratory suit when no claim for conventional relief is ripe. Undoubtedly, obtaining advice about whether contemplated conduct would result in liability is desirable, but giving such advice in advance of actual or imminent conduct is the role of legal counsel, not courts.

Under these principles, there is no ripe controversy here. In stark contrast to mirror-image cases like *Altvater* and *Cardinal*, MedImmune's good standing as a licensee bars Genentech and City of Hope from bringing suit for patent infringement or breach of license. And MedImmune itself lacks any affirmative right of action which would allow it to seek a declaration as an alternative to conventional relief. There would be a ripe justiciable controversy only *if* MedImmune breached or repudiated its license – a contingency that may never occur, since MedImmune's avowed aim is to maintain the license as a shield against suit.

2. Dismissal is also proper on prudential jurisdictional grounds, which this Court may address in the first instance without ruling on the Article III issue – an approach favored by the doctrine of constitutional avoidance. Jurisdiction under the DJA is inherently discretionary and equitable. And under the centuries-old equitable rule of licensee estoppel, MedImmune may not keep the benefits of its license and at the same time attack the validity of the underlying patent in order to escape its license obligations. This kind of one-sided suit is inherently inequitable, because the patentee remains bound by the license and its compromise royalty rate if the attack fails, but the licensee is freed from paying the royalties if it succeeds. Equity demands that the licensee repudiate the license before seeking to invalidate the licensed

patent, thereby maintaining a level playing field between the patentee and the licensee.

*Lear* is consistent with that equitable rule, because the licensee there had repudiated its license before attacking the validity of the underlying patent in court. And, with at most a few scattered exceptions immediately after *Lear*, no court has ever allowed a suit in the present posture. From its creation, moreover, the Federal Circuit has consistently recognized that a licensee cannot attack a patent while keeping the benefits of its license – a rule reaffirmed in *Studiengesellschaft* before the parties entered into the license here.

The question is thus whether a long-standing rule of equity should be abandoned now to allow MedImmune to bring a virtually unprecedented lawsuit. Even if justified by policy considerations, any such change should come from Congress, not the Court. Moreover, policy considerations favor no such change. MedImmune's proposal would seriously impair the core purposes of patent law: to provide incentives for the invention, disclosure, and dissemination of new technologies. Under the MedImmune rule, patentees would have little incentive to enter into one-sided license agreements or (as the United States concedes) would demand exorbitant upfront royalties that would deter technology transfer and raise prices for consumers. That impairment of efficient licensing incentives cannot be justified by an asserted need to free licensees to challenge invalid patents, because the traditional equitable rule and *Lear* already allow such challenges after repudiation. MedImmune's "policy" argument rests on the misconception that the only goal of our patent system is to encourage litigation about patent validity, rather than to provide incentives for innovation. There is no basis here for disturbing settled expectations by permitting a novel, aggressive, and one-sided lawsuit like this.

## ARGUMENT

### I. MedImmune Is Seeking an Advisory Opinion About a Hypothetical Controversy That Is Not Ripe.

#### A. There Must Be A Ripe Claim in Law or Equity Before the Declaratory Procedure May Be Used.

There is no justiciable controversy for declaratory relief here, because none of the parties can presently bring an action for conventional legal or equitable relief. The DJA did not expand the subject-matter jurisdiction of the federal courts. *Skelly Oil Co. v. Phillips Petrol. Co.*, 339 U.S. 667, 671-72 (1950). Rather, "the operation of the Declaratory Judgment Act is procedural only," *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240 (1937), and "merely allow[s] the resolution of a 'case or controversy' in an alternative format." *Calderon v. Ashmus*, 523 U.S. 740, 747 (1998). Hence, the DJA did not accelerate the point at which a controversy becomes ripe for judicial intervention. It must be ripe under the same Article III standards that have always applied to conventional suits.

Article III extends the "judicial Power" to "Cases, in Law and Equity." U.S. Const. art. III, § 2. To the Framers "'[a] case in law or equity ... was a term ... of limited signification.'" *DaimlerChrysler Corp. v. Cuno*, 126 S. Ct. 1854, 1861 (2006) (quoting 4 Papers of John Marshall 95 (C. Cullen ed. 1984)). The Court has "always taken this to mean cases and controversies of the sort traditionally amenable to, and resolved by, the judicial process," *Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 102 (1998), or "matters that were the traditional concern of the courts at Westminster and only if they arose in ways that to the expert feel of lawyers constituted 'Cases' or 'Controversies.'" *Vermont Agency of Nat. Res. v. United States ex rel. Stevens*, 529 U.S. 765, 774 (2000) (quotation marks omitted). Under traditional legal and equitable principles, a controversy is not ripe for

adjudication until an alleged invasion of a legally protected interest has actually occurred, or is at least imminent. *See, e.g., McConnell v. FEC*, 540 U.S. 93, 225-26 (2003). That limitation flows from the very nature of "Cases, in Law and Equity." A legal controversy is generally ripe only after one party has actually invaded the other's legally protected interests, such that an action for damages or other remedy at law lies. Equity extends the judicial power further, to encompass situations when such invasion is imminent – *i.e.*, "certainly impending." *DaimlerChrysler*, 126 S. Ct. at 1863; *McConnell*, 540 U.S. at 225-26. *See generally Woodworth v. Stone*, 30 F. Cas. 593, 594 (C.C.D. Mass. 1845) (Story, J.).[7] But a "claim is not ripe for adjudication if it rests upon contingent future events that may not occur as anticipated, or indeed may not occur at all." *Texas v. United States*, 523 U.S. 296, 300 (1998) (quotation marks omitted). Such a controversy is merely "hypothetical" and not "appropriate for judicial determination." *Aetna*, 300 U.S. at 240.

Consistent with these principles, a controversy is appropriate for resolution in a declaratory action when it has ripened to the point where a conventional suit in law or equity could be brought by one or the other of the parties. Thus, this Court has *never* approved a declaratory suit when there is not a ripe non-declaratory legal or equitable controversy within the meaning of Article III. To the contrary, in its decisions upholding the constitutionality of the declaratory procedure, the Court has emphasized that the DJA simply provides an alternative means of adjudicating disputes that are already within the federal courts' jurisdiction, in one of two ways: either the declaratory judgment defendant has a current right to bring a

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[7] As Justice Story explained, a bill *quia timet* is consistent with these requirements because it requires proof of an "intended violation." *Id.*; *accord Fletcher v. Bealey*, L.R. 28 Ch. D. 688, 698 (1884) ("There must, if no actual damage is proved, be proof of imminent danger . . .").

conventional suit for non-declaratory (legal or equitable) relief, or the declaratory plaintiff has a current right to do so.

### 1. The Potential Defendant to a Ripe Conventional Suit Can File a Mirror-Image Suit for a Declaration of Nonliability.

An important benefit of the declaratory procedure is that it levels the playing field by "allowing prospective defendants to sue to establish their nonliability." *Beacon Theatres, Inc. v. Westover*, 359 U.S. 500, 504 (1959). Before the DJA, a person with alleged liability was powerless to obtain adjudication of a dispute if he did not have his own claim for coercive relief. He was at the mercy of the potential plaintiff, who could sue at any time but might not do so for tactical reasons. The DJA eliminated that one-sidedness by allowing the prospective defendant to turn the tables and initiate a suit for a declaration of nonliability.

*Aetna* exemplifies this kind of "mirror-image" suit. Aetna repeatedly refused to pay insurance claims on the ground that the relevant policies had lapsed. 300 U.S. at 238-39. But the insured did not sue Aetna, so Aetna filed its own action for a declaration that it was not liable. *Id.* at 239. In upholding the declaratory suit, the Court emphasized that the insured presently had ripe conventional claims both for monetary relief and for an equitable decree of nontermination in light of Aetna's repudiation. *Id.* at 243-44. Thus, Aetna was seeking "an adjudication of *present right* upon established facts." *Id.* at 242 (emphasis added). The Court explained that "the character of the controversy and the issue to be determined is essentially the same whether it is presented by the insured or the insurer. . . . It is the nature of the controversy, not the method of its presentation or the particular party who presents it, that is determinative." *Id.* at 244. *Aetna* thus made clear that justiciable controversies are symmetrical, such that Congress could authorize mirror-image suits. But the DJA did not render controversies ripe

and justiciable at any earlier point than for conventional actions.

MedImmune (and the United States) nonetheless argue that *Maryland Casualty* found a declaratory suit justiciable when no conventional suit was ripe. That is incorrect. *Maryland Casualty* actually reiterated *Aetna*'s holding that even where "the declaratory judgment suit" reverses "the positions of the parties in the conventional suit," the Article III "inquiry is the same in either case." *Md. Cas. Co. v. Pac. Coal & Oil Co.*, 312 U.S. 270, 273 (1941). Consistent with that principle, the declaratory defendant in *Maryland Casualty* did have ripe conventional claims against the declaratory plaintiff. The case involved the recurring fact pattern in which an injured person sues an insured but not its insurer, and then the insurer brings a declaratory action against both the injured person and the insured to determine whether the insurer has an obligation to defend and pay any judgment. *Id.* at 271-72. That is the mirror image of the ripe affirmative suit that an injured party could *presently* bring under federal procedure against both the insured and its insurer. *See* Fed. R. Civ. P. 18(b) (permitting joinder of insurer as defendant before adjudication of insured's primary liability); *see also* Fed. R. Civ. P. 14 (impleader procedure).[8] Thus, there was a ripe conventional controversy in *Maryland Casualty*. The Court therefore allowed the mirror-image suit under the DJA and, indeed, emphasized that the "inquiry is

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[8] In finding a ripe controversy, *Maryland Casualty* followed *United States Fidelity & Guaranty Co. v. Pierson*, 97 F.2d 560 (8th Cir. 1938) (cited 312 U.S. at 273), which explained that the injured party has a ripe conventional claim against the insurer because the insurer's liability *vel non* depends only on actually existing facts and, indeed, the insurer is the real party in interest in the injured party's suit against the insured. 97 F.2d at 562. MedImmune's misreading of *Maryland Casualty* is based on the *state procedure* that prevented the injured party from immediately suing the insurer in state court. But state procedures are not controlling under the DJA. *Skelly Oil*, 339 U.S. at 673-74.

the same" in conventional and declaratory suits. 312 U.S. at 273.

### 2. A Plaintiff with a Ripe Conventional Claim Can Seek a Declaration as Alternative Relief.

Not all declaratory actions are the mirror images of conventional suits. A ripe controversy also exists when the declaratory *plaintiff* can presently sue for a coercive judgment, but chooses to seek declaratory relief instead of, or in addition to, seeking money damages or an injunction. In such "alternative relief" actions, the case or controversy arises from an actual or imminent invasion of the plaintiff's own legal interests, rather than from an invasion of the defendant's interests as in a mirror-image declaratory action.

Suits for declarations that laws are unconstitutional, such as *Steffel v. Thompson*, 415 U.S. 452 (1974), are justiciable on this "alternative relief" basis. Controversies of this kind are ripe because the declaratory plaintiff can presently bring a conventional action to enjoin enforcement of the unconstitutional law. The plaintiff may therefore use the declaratory procedure to seek a declaration of unconstitutionality as an alternative to injunctive relief. The Court emphasized this in its first decision upholding the declaratory procedure, in a suit for a declaration that a state tax unconstitutionally burdened interstate commerce. *Nashville, Chattanooga, & St. Louis Ry. v. Wallace*, 288 U.S. 249 (1933). In his opinion for a unanimous Court, Justice Stone framed the issue thus:

> [T]he narrow question presented for determination is whether the controversy before us, which would be justiciable in this Court if presented in a suit for injunction, is any the less so because through a modified procedure appellant has been permitted to present it . . . without praying for an injunction . . . .

*Id.* at 262-63. So framed, the answer was clear: the form of relief did not affect the ripeness of the suit. *Id.* at 263.

The Court made the same point in *Steffel*, which stressed that declaratory relief against unconstitutional laws is simply an alternative to injunctive relief under *Ex parte Young*, 209 U.S. 123 (1908), pursuant to the right of action created by Congress in 42 U.S.C. § 1983. *Steffel*, 415 U.S. at 464-66. *Steffel* also reiterated the settled doctrine, which can be traced back at least to *Young* itself, that this equitable jurisdiction exists even if the plaintiff complies with the law to avoid prosecution. In that situation, the official's threat to enforce the unconstitutional law is a *present* invasion of the plaintiff's own legally protected rights, analogous to trespass, which creates a ripe controversy regardless of whether the plaintiff complies with the law or defies it. *Young*, 209 U.S. at 155-56, 158, 167; *Steffel*, 415 U.S. at 459 (where person complies with unconstitutional law to avoid prosecution, threat of enforcement "deters the exercise of his constitutional rights"); *Lake Carriers' Ass'n v. MacMullan*, 406 U.S. 498, 508 (1972) (when "compliance is coerced by the threat of enforcement, ... the controversy is both immediate and real").[9] In these cases, then, declaratory relief is simply an alternative "to the strong medicine of the injunction." *Steffel*, 415 U.S. at 466-68 & n.18; *see* S. Rep. No. 73-1005, at 3 (1934).[10]

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[9] Likewise, pre-enforcement review of agency regulations is justiciable under the Administrative Procedure Act when "the expected conformity to them causes injury cognizable by a court of equity." *Abbott Labs. v. Gardner*, 387 U.S. 136, 150 (1967) (quotation marks omitted).

[10] The existence of equity *jurisdiction* in these cases does not mean an injunction would necessarily be granted *on the merits*. Because declaratory relief is less intrusive, it may be available when an injunction is denied on the merits, such as when the imminent injury to the plaintiff's rights is not irreparable or an injunction would undermine comity. *Nashville*, 288 U.S. at 264; *Steffel*, 415 U.S. at 468-73. But as in any other case in which relief is denied on the merits, the denial of

MedImmune (and the United States) fundamentally misread cases like *Steffel* as if they were mirror-image declaratory actions like *Aetna*. From that false perspective, they argue that such controversies are ripe merely because the *defendant* government official *would be able to* bring an enforcement action against the declaratory plaintiff *if* the plaintiff defied the law – which they analogize to Genentech's and City of Hope's hypothetical ability to sue MedImmune if MedImmune repudiated its license. But as Justice Stone explained more than 70 years ago, these constitutional challenges are justiciable because the plaintiff can presently sue for traditional equitable relief, *Nashville*, 288 U.S. at 263, not because of any hypothetical suit that the defendant might be able to bring under conditions that have not and may never come to pass. Properly understood, *Steffel* cannot be analogized to this case because MedImmune, as plaintiff, lacks a ripe claim for conventional relief against Respondents. *Infra* at 25-29.

### 3. MedImmune's Reliance on Lower Court Decisions and Legislative History Is Misplaced.

Ignoring this Court's admonishments that the Article III inquiry is identical regardless of whether declaratory or conventional relief is sought, MedImmune (and the United States) cite lower court cases which they characterize as allowing declaratory actions for interpretations of contracts in advance of breach, repudiation, or other actual or imminent conduct that would ripen a conventional contract suit. Initially, the impression Petitioner tries to create that such cases are legion does not correspond to reality. Contract cases (other than insurance coverage disputes like

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injunctive relief is irrelevant to whether there is a justiciable controversy in the first place. By the same token, a declaratory action would never be an available alternative in situations where an injunctive suit is barred on ripeness grounds – such as when the plaintiff wants to challenge the constitutionality of a law that is not enforced.

*Aetna* and *Maryland Casualty*) represent a small fraction of the declaratory suits filed in federal court, presumably because such cases are governed by state law and federal jurisdiction ordinarily is lacking, *Skelly Oil*, 339 U.S. at 671-74.[11] To the extent declaratory contract cases are filed in federal court, many are in fact justiciable under the traditional Article III standards described above. Indeed, even after cherry-picking the lower court decisions that most closely favor its own theory, MedImmune cites several cases that do not support its position because there were ripe claims for conventional relief at the time declaratory relief was sought. *E.g.*, *Duane Reade Inc. v. St. Paul Fire & Marine Ins. Co.*, 411 F.3d 384, 387 (2d Cir. 2005) (cited at Pet'r Br. 20) (plaintiff had ripe conventional claim for breach of insurance policy); *NUCOR Corp. v. Aceros y Maquilas de Occidente, S.A. de C.V.*, 28 F.3d 572, 578 (7th Cir. 1994) (cited at Pet. 15-16) (defendant had ripe conventional claims for deceptive trade practices and breach of contract); *see also infra* at 38 & note 20 (discussing patent license cases).

To be sure, there are some other cases where lower courts have adjudicated declaratory claims in the absence of a ripe conventional controversy under Article III. But MedImmune cannot cite a single case in which *this Court* has allowed a declaratory suit in such circumstances. The reason is clear: a suit to find out whether a party *would* breach its contract *if* it engaged in certain conduct inherently seeks legal advice about facts that are hypothetical, not actual or imminent – "contingent future events that may not occur as anticipated,

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[11] Thus, these cases can be heard in state court if the state law that governs them provides for such resolution. If not, it is hard to see what harm is done by keeping state law cases that cannot be heard in state court out of federal court too. *See, e.g., 118 E. 60th Owners, Inc. v. Bonner Props., Inc.*, 677 F.2d 200, 204-06 (2d Cir. 1982) (cited at Pet'r Br. 20) (declining jurisdiction over declaratory claim governed by state law where precluded by state procedure).

or indeed may not occur at all." *Texas*, 523 U.S. at 300 (quotation marks omitted). Undoubtedly, obtaining advice about whether contemplated conduct would result in liability is desirable, but giving such advice in advance of decisions about whether to breach is the role of legal counsel, not courts. Though lower courts may have sometimes allowed declaratory suits about hypothetical or contemplated conduct when no conventional suit could be brought, this Court has never crossed that threshold and should not do so now.

In fact, this case is a particularly poor candidate for even considering adjudication of hypothetical rights based on MedImmune's assertion that it is burdened by having to decide whether to repudiate the license before knowing for certain the legal status of the Cabilly II Patent. Assuming *arguendo* that such prudential considerations could *expand* the jurisdiction of federal courts beyond the historical parameters encapsulated in Article III, MedImmune's suit still could not be allowed. As Genentech shows in its brief, this suit is fundamentally different from declaratory suits on ordinary contracts where uncertainties about the meaning of the contract itself have arisen after it is signed. Here, the very uncertainty about which MedImmune complains was built into the terms of the deal. For that and other reasons, prudential and equitable principles require dismissal of MedImmune's claims, not their immediate adjudication. *Infra* at 32-50.

MedImmune also cites legislative history suggesting that congressional committees thought declaratory suits could be brought to interpret contracts without breach. But suits outside the scope of Article III cannot be authorized by statute – much less by legislative history. Just as importantly, MedImmune ignores Congress's overarching intent in enacting the DJA – expressed in the statute's actual language as well as the legislative history – to confine declaratory actions to "actual controvers[ies]" within Article

III's limits. 28 U.S.C. § 2201; *see* S. Rep. No. 73-1005, at 5 (1934). By expressly limiting the DJA to "actual controversies," Congress intended it to be "operative only in respect to controversies which are such in the constitutional sense," *Aetna*, 300 U.S. at 240, and so did "not attempt to change the essential requisites for the exercise of judicial power." *Ashwander v. TVA*, 297 U.S. 288, 325 (1936). That congressional intent excludes lawsuits about hypothetical circumstances, particularly where the supposed right to seek a judicial declaration is entirely asymmetrical, with the patentee barred by a license from suing the licensee. The DJA was never intended to create that kind of unfair disparity. *See Franchise Tax Bd. v. Constr. Laborers Vacation Trust*, 463 U.S. 1, 19 n.19 (1983) ("the declaratory remedy . . . was designed to permit adjudication of either party's claim of right").[12]

**B. No Conventional Suit – and Thus No Declaratory Suit – Is Ripe Here.**

Under these established principles, there is no ripe controversy here. Because MedImmune has no intention of repudiating its license, it has prevented the ripening of any suit against it for patent infringement or breach of license. Therefore MedImmune cannot bring a mirror-image declaratory action to establish that it would not be liable *if* it repudiated the license. Nor has Congress given parties like MedImmune any substantive rights whose invasion would allow MedImmune to seek a declaration as an alternative to coercive relief. As long as MedImmune remains an

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[12] The only apparent exception to the symmetry of declaratory rights of action is for suits to declare laws unconstitutional, such as *Steffel*. For prudential reasons, government officials ordinarily cannot sue in reverse to have a law declared constitutional. *See Franchise Tax Bd.*, 463 U.S. at 21 ("States are not significantly prejudiced by an inability to come to federal court for a declaratory judgment in advance of a possible injunctive suit by a person subject to federal regulation").

authorized user rather than an infringer, there can be no justiciable controversy.

### 1. Mirror-Image Suits Are Important in Patent Law, But Cannot Be Brought When a License Bars Any Suit by the Patentee.

Mirror-image declaratory suits play an important role in patent law. Before the DJA, a patentee could engage in the "*danse macabre*" of accusing competitors of infringement but never filing suit, thus forcing the competitors to choose between incurring a growing potential liability for infringement or abandoning their businesses. *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 95-96 (1993). The patentee might even file suit for its *in terrorem* effect, but then dismiss it prior to judgment. *See* Edwin Borchard, *Declaratory Judgments* 43, 802-08, 812-16 (2d ed. 1941). The DJA ended these strategies. If the patentee can presently sue, the potential infringer can seize the initiative with a mirror-image declaratory suit. *Cardinal*, 508 U.S. at 96; *see also Walker Process Equip., Inc. v. Food Mach. & Chem. Corp.*, 382 U.S. 172, 176 (1965) (under DJA, accused infringer "need not await the filing of a threatened suit by the patentee"). Similarly, after being sued, accused infringers can assert declaratory counterclaims to prevent unilateral dismissal by the patentee. *Cardinal*, 508 U.S. at 96.

*Altvater* and *Cardinal* exemplify the latter situation. In each case, the patentee first filed a conventional suit for legal or equitable relief against accused infringers, who then filed counterclaims for declarations of patent invalidity. *Altvater v. Freeman*, 319 U.S. 359, 360-61 (1943); *Cardinal*, 508 U.S. at 85-86. As the patentees had already filed conventional suits, these were plainly ripe controversies. *Cardinal*, 508 U.S. at 96 ("If . . . a party has actually been charged with infringement of the patent, there is, *necessarily*, a case or controversy adequate to support jurisdiction of a complaint, or a counterclaim, under the" DJA); *Altvater*, 319

U.S. at 363 ("the issue of validity may be raised by a counterclaim in an infringement suit").[13]

Here, however, MedImmune has forestalled the ripening of any justiciable controversy through its deliberate strategy of maintaining its good standing as a licensee. This case is therefore fundamentally different from *Altvater* and *Cardinal*, where the patentees not only *could* sue, but had actually done so. MedImmune's avowed intent to maintain its license forestalls any such suit. *See Textron Lycoming Reciprocating Engine Div. v. United Auto. Workers of Am., Int'l Union*, 523 U.S. 653, 662-63 (1998) (opinion of Breyer, J.) (for mirror-image declaratory action to be ripe, actionable conduct by plaintiff must at least be imminent).[14]

MedImmune (and the United States) nonetheless argue that *Altvater* is exactly like this case because the alleged infringer there was making royalty payments to the patentee. But that ignores the essential distinction. In *Altvater* – unlike this case – the payments did not negate the patentee's claims. First, the patentee alleged that the former licensee had

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[13] *Altvater* and *Cardinal* also addressed the distinct issue of whether a declaratory counterclaim of patent invalidity becomes moot on appeal after rejection of the patentee's infringement claim – the central question in both cases. 319 U.S. at 363-64; 508 U.S. at 96. *Cardinal* made clear, however, that mootness on appeal is entirely distinct from whether there is a live controversy to support the filing of a declaratory invalidity claim in the first instance. 508 U.S. at 95-98; *cf. Friends of the Earth, Inc. v. Laidlaw Envt'l Servs. (TOC), Inc.*, 528 U.S. 167, 189-92 (2000).

[14] There is also no merit to the suggestion of some *amici* that *Respondents* could file their own declaratory suit to establish the validity of their patent. Such a suit by the patentee would simply break out a single issue relevant to the patentee's own potential cause of action for infringement, which is what this Court held a declaratory plaintiff may not do in *Calderon*, 523 U.S. at 747. Moreover, patents are presumed valid until proven otherwise, 35 U.S.C. § 282, and a court may hold only that a patent has not been proved invalid, not that it is valid. *See, e.g., Shelcore, Inc. v. Durham Indus., Inc.*, 745 F.2d 621, 627 (Fed. Cir. 1984).

breached the license in other ways, by manufacturing and selling patented products prohibited by the license. 319 U.S. at 360. Second, the license had terminated in any event. *Id.* at 362. Third, the royalties were paid under an injunction, not to maintain the protection of the (terminated) license against suit. *Id.* at 365. For these reasons, payment of royalties did not bar a suit by the patentee. Thus, the United States' attempt to liken *Altvater* to this case by asserting that the alleged infringer in *Altvater* could not be sued (U.S. Br. 18) is simply mystifying. Not only could the patentee sue in *Altvater*, it had in fact done so by initiating the litigation.

In truth, MedImmune's aggressive litigation strategy is virtually unprecedented even in the lower courts. *Infra* at 38 & note 20 (discussing cases). That is unsurprising, because in this context any potential justiciable controversy is either moot or unripe. Before the license, there could have been a case or controversy if MedImmune had actually or imminently engaged in conduct that could be infringing. But the license mooted any such potential controversy. On the other hand, a new controversy could arise if MedImmune took actions that breached the license. But such a suit is not yet ripe (and may never be). MedImmune has not taken such action and has disclaimed any intention of doing so.

**2. Congress Has Not Given MedImmune Its Own Right of Action for Affirmative Conventional Relief.**

It is equally clear that there is no ripe claim for legal or equitable relief that MedImmune could assert against Genentech or City of Hope, which would allow MedImmune to seek declaratory relief as an alternative to damages or an injunction. In fact, Congress has steadfastly refused to give affirmative rights of action to parties like MedImmune. MedImmune's broadsides against the Patent Act's remedial scheme and the PTO's handling of patent applications and reexaminations are nothing but blatant appeals for this Court

to second-guess Congress and supplant the executive officials it has charged with administrative functions.

Congress has vested executive officials in the PTO with the authority to examine patent applications and issue patents when the statutory requirements for patentability are met, 35 U.S.C. § 131, and authority to reexamine previously granted patents under statutorily enumerated conditions, *id.* §§ 301-318, and has also authorized the applicant or patentee to seek judicial review of denial of its application or an adverse decision on reexamination, *id.* §§ 141, 306, 315(a). Further, Congress has defined "infringe[ment]" as the act of practicing a patent "without authority," *id.* § 271(a); given the patentee a "remedy by civil action for infringement of a patent," *id.* § 281; and authorized conventional legal and equitable relief against infringers to protect that core substantive right, *id.* §§ 271, 281-285. Noninfringement, invalidity, and unenforceability are *defenses* to an infringement suit. *Id.* § 282. But, except for narrow statutory exceptions not at issue here, Congress has not created any express or implied right of action by which interested private persons who cannot be sued for infringement may test the validity or enforceability of a patent. *Mowry v. Whitney*, 81 U.S. (14 Wall.) 434, 439-41 (1872); *United States v. Am. Bell Tel. Co.*, 128 U.S. 315, 368-73 (1888); *United States v. Glaxo Group Ltd.*, 410 U.S. 52, 65 (1973) (Rehnquist, J., dissenting); *Christianson v. Colt Indus. Oper. Corp.*, 486 U.S. 800, 808 & n.2 (1988) (Stevens, J., concurring) ("I find no merit in respondent's suggestion that we should recognize an implied cause of action" to enforce patentability requirements).[15]

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[15] The two statutory exceptions to this rule are for (1) civil interference actions initiated by one patentee or applicant against another (the procedure utilized by Genentech against Celltech, *see supra* at 3-4), 35 U.S.C. § 146; and (2) judicial review by a third-party requester of a PTO decision upholding a patent in an administrative *inter partes*

It is up to Congress – not the courts – to decide whether to create new substantive rights (something Congress did not do in the purely procedural DJA, *e.g.*, *Beacon*, 359 U.S. at 509). When Congress creates new rights, their actual or imminent invasion can give rise to a justiciable controversy where none would otherwise exist. *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 580 (1992) (opinion of Kennedy, J.) ("Congress has the power to define injuries and articulate chains of causation that will give rise to a case or controversy where none existed before"). Congress has in fact exercised that power in the Patent Act as it applies to generic drugs – but not here. Congress provided that the mere filing of an application for regulatory approval to market a generic drug in advance of the expiration of a relevant patent is an act of infringement, which allows the patentee immediately to bring a suit for injunctive relief. 35 U.S.C. § 271(e)(2)-(4); *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 665-67 (1990) (explaining this "artificial" act of infringement). And when a suit for infringement accrues in that situation, a mirror-image declaratory suit may also be ripe. 35 U.S.C. § 271(e)(5) (authorizing mirror-image declaratory suits in this context after 45 days). Thus, by giving patentees a new substantive right, Congress created a system for early adjudication of generic drug patent disputes when that right is invaded.

Congress also could have given patent licensees new substantive rights on which to bring suit, even absent claims against them for infringement. For example, Congress might have created a cause of action against patentees who request royalty payments where the patent is invalid – a claim that

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reexamination proceeding (which Congress did not extend to preexisting patents such as Cabilly II), *id.* § 315(b); Pub. L. No. 106-113, tit. IV, § 4608(a), 113 Stat. 1501, 1536, 1501A-572 (1999) (effective date). The narrowness of the express exceptions drives home that there is no general right of interested persons to challenge a patent.

could be ripe even if the license barred the patentee from suing. But Congress has not done so.

For that reason, this suit is fundamentally different from pre-enforcement challenges to the constitutionality of statutes like *Steffel*. Those cases involve invasion of the plaintiff's own substantive rights that the Constitution itself guarantees, and they are brought pursuant to the cause of action created by Congress in § 1983. *See supra* at 17-19. In that context, the DJA merely supplies an alternative procedure and form of relief for a suit the plaintiff could already bring to vindicate his preexisting rights. That is a far cry from the situation here, where the only substantive rights created by Congress belong to Respondents, not MedImmune, and the license negates any controversy relating to those rights.[16]

Restricting the judicial power to justiciable controversies "is crucial in maintaining the tripartite allocation of power set forth in the Constitution." *DaimlerChrysler*, 126 S. Ct. at 1861 (quotation marks omitted). That is certainly true here. Article III's requirements preserve the statutory patent regime enacted by Congress and the authority it confers on the Executive, by ensuring that the judiciary does not inject itself into a disagreement about patent validity or enforceability except when properly presented as part of fully ripe controversy suitable for judicial resolution. As this Court emphasized 140 years ago, if "an individual finds himself injured" by an allegedly invalid patent, "it is no hardship to require him" to seek relief from executive officials. *Mowry*, 81 U.S. at 441. But allowing any interested person to sue in court to invalidate the patent "would tend to discredit the authority of the government in

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[16] Nor may MedImmune leverage its justiciable (but meritless) antitrust claims to sustain its declaratory patent claims on an ancillary jurisdiction theory. The requirements of Article III must be separately satisfied for each claim in a complaint. *DaimlerChrysler*, 126 S. Ct. at 1866-68.

such matters" – and "seriously impair the value of the title which the government grants after regular proceedings before officers appointed for the purpose." *Id.*

### 3. "Reasonable Apprehension of Suit" Is Not at Issue Here.

Consistent with the foregoing, the Federal Circuit correctly reasoned that this suit is not ripe because "MedImmune is complying fully with the license terms and cannot be sued by the patentee[s]." Pet. App. 5a. Unfortunately, the Federal Circuit then confused matters by invoking "reasonable apprehension of suit." *Id.* at 7a-9a. The impossibility of the patentee suing negates any justiciable controversy. It is thus unnecessary to inquire whether, in addition, the licensee also has a "reasonable apprehension" of being sued.

This is made clear by considering both prongs of the Federal Circuit's test for the ripeness of declaratory suits: "First, the plaintiff must actually produce or be prepared to produce an allegedly infringing product. Second, the patentee's conduct must have created an objectively reasonable apprehension on the part of the plaintiff that the patentee will initiate suit if the activity in question continues." *EMC Corp. v. Norand Corp.*, 89 F.3d 807, 811 (Fed. Cir. 1996); *see also* Pet. App. 7a. The first prong of this test goes to the justiciability requirement at issue here: whether the declaratory plaintiff is actually or imminently engaging in allegedly infringing conduct, which allows the patentee to bring an infringement suit now. If not, there is no ripe controversy, and the inquiry is at an end. The second prong relating to "reasonable apprehension" comes into play only as an additional requirement if the potential infringer can be sued under the first prong. *See, e.g.*, *EMC*, 89 F.3d at 811. As the first prong is not satisfied here, "reasonable apprehension" is irrelevant.

The briefs of MedImmune and its *amici* nonetheless brim with critiques of the Federal Circuit's application of the "reasonable apprehension" prong in cases where the patentee *can* sue, but refuses to do so. These arguments might well raise questions that merit the Court's attention in some future case where they are presented – although there are certainly counterarguments.[17] But those questions are not presented here. This case has nothing to do with scenarios in which the patentee refuses to sue for strategic reasons, or makes veiled threats of suit that do not create a "reasonable apprehension" under the Federal Circuit's application of its standard. There is no ripe controversy here because MedImmune has deliberately precluded Respondents from suing – not because of any strategic conduct by Genentech or City of Hope.

### C. This Suit Also Is Not Justiciable Because MedImmune Lacks Standing.

MedImmune also does not satisfy the "actual injury" test for Article III standing. Of course, the ripeness defects discussed above are dispositive, whether or not MedImmune had standing. Justiciability requires "not only the standing of litigants to assert particular claims, but also the appropriate timing of judicial intervention." *Renne v. Geary*, 501 U.S. 312, 320 (1991); *accord DaimlerChrysler*, 126 S. Ct. at 1867 ("The doctrines of mootness, ripeness, and political question all originate in Article III's 'case' or 'controversy' language, no less than standing does"). Thus, a dispute may be dismissed as unripe even when a plaintiff has standing.

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[17] For example, despite his broad view of declaratory relief, Professor Borchard emphasized that "in a suit by the alleged infringer of a patent against the patentee for a declaration that the petitioner is not infringing or that the defendant's patent is invalid, *a threat or claim of infringement emanating from the patentee* to the petitioner or his customers is *always necessary*" in order to "refute[] the fear that patentees might be harassed by prospective infringers and be obliged continually to defend their patents." Borchard, *Declaratory Judgments* at 43, 807 (emphasis added).

*Compare Renne*, 501 U.S. at 319-20 (finding standing), *with id.* at 320-23 (dismissing for lack of ripeness).

MedImmune lacks standing because it has not "suffered an 'injury in fact,'" or "the invasion of a legally protected interest" with a proximate "causal connection" to the conduct of Respondents. *Lujan*, 504 U.S. at 560. Although standing does not depend on the merits, "it often turns on the nature and source of the claim asserted." *Warth v. Seldin*, 422 U.S. 490, 500 (1975). The absence of Article III injury here is in part related to the point, discussed above, that in the Patent Act Congress gave substantive rights to patentees, not licensees or other hypothetical infringers. *See supra* at 26-28. Thus, MedImmune's claim of injury is "not to a legally cognizable right." *McConnell*, 540 U.S. at 227.

Indeed, far from being "injured" by Respondents, MedImmune has the unilateral power to decide whether to repudiate its license and stop paying royalties. *Infra* at 33-49. MedImmune has not done so because it wants to retain the license as a shield against suit – something Respondents are powerless to prevent. As Genentech explains at greater length in its brief, that kind of voluntary "personal choice" by the plaintiff cannot constitute an injury proximately caused by the defendant. *McConnell*, 540 U.S. at 228.

Nor can MedImmune satisfy the injury in fact requirement by arguing that it *might* be held liable for infringement *if* it repudiated the license. Even assuming that being held liable for committing a wrong against another private party could ever count as an injury to a legally protected interest – which seems dubious – any such possibility is entirely contingent and remote here. Since MedImmune will not repudiate its license, there is no "injury" of this kind. *Lujan*, 504 U.S. at 560 (injury must be actual or imminent, not conjectural or hypothetical).

## II. Even Assuming Article III Allowed this Suit, Dismissal Should Be Affirmed on Prudential Grounds.

### A. Jurisdiction Under the DJA Is Subject to Prudential and Equitable Limitations.

Even aside from the absence of an Article III controversy, prudential and equitable considerations bar the exercise of jurisdiction here. Like the other doctrines that cluster around "case or controversy," ripeness has a prudential dimension. *Reno v. Catholic Soc. Servs., Inc.*, 509 U.S. 43, 57 & n.18 (1993); *Renne*, 501 U.S. at 325 (Stevens, J., concurring). In addition to the bedrock requirements of Article III, courts must "evaluate . . . the hardship to the parties of withholding court consideration" before finding a case ripe. *Texas*, 523 U.S. at 301 (quotation marks omitted).

Prudential considerations apply with especial force to declaratory claims, where jurisdiction is inherently discretionary. 28 U.S.C. § 2201 (court "may" hear claim for declaratory relief). "The Declaratory Judgment Act was an authorization, not a command. It gave the federal courts competence to make a declaration of rights; it did not impose a duty to do so." *Public Affairs Assocs., Inc. v. Rickover*, 369 U.S. 111, 112 (1962). Thus, courts "possess discretion in determining whether and when to entertain an action under the Declaratory Judgment Act, even when the suit otherwise satisfies subject matter jurisdictional prerequisites." *Wilton v. Seven Falls Co.*, 515 U.S. 277, 282 (1995).

Exercises of that discretion must be guided by principles of equity:

> Congress . . . explicitly contemplated that the courts would decide to grant or withhold declaratory relief on the basis of traditional equitable principles. . . . [I]n an action for a declaratory judgment, the district

> court [is] as free as in any other suit in equity to grant or withhold the relief prayed, upon equitable grounds.

*Samuels v. Mackell*, 401 U.S. 66, 70 (1971) (quotation marks omitted); *accord Abbott Labs. v. Gardner*, 387 U.S. 136, 155 (1967); *Rickover*, 369 U.S. at 112. And when equity bars the suit, the proper response is for the court to decline to exercise jurisdiction at the outset. *Wilton*, 515 U.S. at 287-88. Indeed, the discretionary aspect of the DJA is tied to ripeness requirements for subject matter jurisdiction. *Catholic Soc. Servs.*, 509 U.S. at 57-58; *Abbott Labs.*, 387 U.S. at 148-49.

Categorical rules may govern the courts' equitable discretion to decline DJA jurisdiction in appropriate cases. *See Martin v. Franklin Capital Corp.*, 126 S. Ct. 704, 710 (2005) ("limiting discretion according to legal standards helps promote the basic principle of justice that like cases should be decided alike"); *Rickover*, 369 U.S. at 112. While equity sometimes requires fact-specific balancing of multiple factors by the trial court, reviewed for abuse of discretion, *e.g.*, *eBay, Inc. v. MercExchange, L.L.C.*, 126 S. Ct. 1837, 1839 (2006); *Wilton*, 515 U.S. at 282-83, 288-89, a rule of equity may govern an entire category of cases when a single consideration is decisive and no balancing is required. *See Wilton*, 515 U.S. at 289 (referring to "the exercise of 'judicial discretion, hardened by experience into rule'") (quoting Borchard, at 293). Such categorical rules govern declaratory jurisdiction in many cases. *E.g.*, *Samuels*, 401 U.S. at 68-73 (*Younger* abstention, which sounds in equity, applies to declaratory actions); *Cardinal*, 508 U.S. at 102-03.

### B. Equity Bars a Licensee from Simultaneously Challenging a Patent's Validity and Keeping the Benefits of Its License for that Patent.

Under the long-standing rule of equity known as licensee estoppel, MedImmune cannot challenge the validity or enforceability of Cabilly II as long as it seeks to retain the

benefits of its license for that patent. A licensee in good standing shares in the property rights granted by the patent, because the licensee receives the right to use the invention without being threatened with infringement liability and benefits from the patent's exclusion of others from doing the same. *E.g.*, *Lear*, 395 U.S. at 669 & n.16. It would be inequitable under any circumstances to allow a licensee to continue laying claim to those rights and at the same time attack the patent that underlies them. But the inequity is especially great where, as here, the licensee seeks to preserve its favorable royalty rate at the same time it sues, so that it can keep the benefits of the license if it loses its lawsuit but escape its contractual obligation to pay royalties if it wins.

**1. Under Traditional Equity Principles, a Licensee Must Repudiate the License Before Challenging the Underlying Patent.**

Licensee estoppel has ancient roots and is derived from the even more venerable doctrine of lessee estoppel. *E.g.*, *Hayne v. Maltby*, 100 Eng. Rep. 665, 666-67 (K.B. 1789); *Taylor v. Hare*, 127 Eng. Rep. 461, 462 (C.P. 1805); *Cutler v. Bower*, 116 Eng. Rep. 736, 741 (K.B. 1848). *See generally* William C. Rooklidge, *Licensee Validity Challenges and the Obligation to Pay Accrued Royalties* (Part I), 68 J. Pat. & Trademark Off. Soc'y 506 (1986); *id.* (Part II), 69 J. Pat. & Trademark Off. Soc'y 5 (1987). In the first American licensee estoppel case, the court relied on the analogy to landlord-tenant law and explained that the estoppel equitably arises from the licensee's enjoyment of the fruits of the licensed property. *Wilder v. Adams*, 29 F. Cas. 1216, 1217-18 (C.C.D. Mass. 1846). Less than a decade later, this Court adopted the rule on the same grounds. *Kinsman v. Parkhurst*, 59 U.S. 289, 292-93 (1855); *see Lear*, 395 U.S. at 663 (recognizing that *Kinsman* "invoked estoppel in a considered manner").

Licensee estoppel is a rule of equity, not contract. It bars the licensee from attacking the patentee's title only as long as the licensee seeks to continue benefiting from the patent through the license – regardless what the license contract provides. Thus, even if a license prohibits the licensee from challenging patent validity or terminating the license as a matter of contract law, the rule of equity allows the licensee who believes that the patent is invalid to escape its contract obligations by *repudiating* the license and asserting invalidity in subsequent litigation. *See* Rooklidge (Part I), 68 J. Pat. & Trademark Off. Soc'y at 515-16, 519-22. Licensee estoppel is therefore more liberal to the licensee than ordinary contract rules, which do not allow a party to escape its bargain by repudiation.

In *St. Paul Plow-Works v. Starling*, 140 U.S. 184 (1891), for example, the licensee gave notice that it "renounced its license and all claim of right to construct plows in accordance with the plaintiff's patent." *Id.* at 186. The Court held that this repudiation did *not* terminate the license under contract law. *Id.* at 195. Nonetheless, having surrendered the benefits of the license, the repudiating licensee was not estopped from contesting the patent's validity as a defense. *Id.* at 196-98. In contrast, the United States as licensee was estopped from raising an invalidity defense in *United States v. Harvey Steel Co.*, 196 U.S. 310, 316 (1905), because the licensee "did not rescind the contract or give a notice which would have put the claimant on its guard, or enabled it to proceed against the manufacturers, but stood silent until the work was done and [the licensee] had received the fruits of [its] agreement." *Harvey Steel Co. v. United States*, 38 Ct. Cl. 662, 685 (1903), *aff'd*, 196 U.S. 310 (1905). Thus, as one oft-cited case explained, a licensee is estopped from denying the validity of the patent

> unless, prior to the period for which the royalties are sought to be recovered, he has given to the licensor a

> distinct, definite, and unequivocal notice to the effect that he no longer recognizes the binding force of the agreement, and that he will thereafter manufacture or use the article covered by the patent under a claim of right, founded upon the alleged invalidity of the patent, and in hostility to and defiance of the authority of the patent and the license, so that the licensor can thereafter proceed against him for an infringement of the patent, if he chooses to do so.

*Martin v. New Trinidad Lake Asphalt Co.*, 255 F. 93, 94 (D.N.J. 1919).[18]

This "repudiation limitation place[s] both parties to the license agreement in an equitable position." Rooklidge (Part II), 69 J. Pat. & Trademark Off. Soc'y at 9. It bars the licensee "from challenging validity as long as he accept[s] the benefits of the license" but not "[o]nce the licensee repudiate[s] the license," because then "he not only g[ives] up any exclusive or deterrent effect, but also expose[s] himself to an infringement suit." Rooklidge (Part I), 68 J. Pat. & Trademark Off. Soc'y at 522.

### 2. *Lear* Was a Repudiation Case, and Its Holding Is Consistent with the Historical Equity Rule.

In the mid-20th century, however, a few cases held that licensee estoppel continued even after repudiation, and that misconception crept into this Court's opinions. In *Automatic Radio Manufacturing Co. v. Hazeltine Research, Inc.*, 176 F.2d 799 (1st Cir. 1949), *aff'd*, 339 U.S. 827 (1950), the lower court held that estoppel continued until the license itself was terminated according to its terms under contract law, regardless of repudiation by the licensee. 176 F.2d at

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[18] Similarly, even if a license has not been terminated under contract law, the licensee may challenge the patent if he has been "evicted" by a final court decision in favor of a third party holding that the patent is invalid. *See* Rooklidge (Part I), 68 J. Pat. & Trademark Off. Soc'y at 513-15.

809-10. Affirming, this Court stated the "general rule . . . that the licensee under a patent license agreement may not challenge the validity of the licensed patent," without noting that estoppel ends with repudiation. *Automatic Radio Mfg. Co. v. Hazeltine Research, Inc.*, 339 U.S. 827, 836 (1950).

*Lear* reflected *Hazeltine*'s confusion. The licensee in *Lear* became convinced that the licensed patent application was fully anticipated and invalid and so gave notice to the patentee and stopped paying royalties. 395 U.S. at 659-60. When the patentee sued for breach of license, the licensee argued – consistent with the traditional rule of equity – that "a licensee may escape the impact of estoppel simply by announcing that it has repudiated the licensing agreement, regardless of the contract's terms." *Id.* at 662 n.10. But the California Supreme Court held that the estoppel still applied, because the license "had not been validly terminated" under contract law. *Adkins v. Lear, Inc.*, 435 P.2d 321, 331 (Cal. 1967), *rev'd*, 395 U.S. 653 (1969).

That abandonment of the traditional scope of licensee estoppel truly "muzzled" the licensee as a potential challenger of the suspect patent's validity. *Lear*, 395 U.S. at 670. If (as in *Lear*) the license itself prohibited termination, then it could *permanently* estop the licensee from attacking the patent until it expired. That might be a reasonable rule of contract law, but it is not the traditional rule of equity that allows the licensee to escape its license obligations by repudiating its license benefits.

Thus, this Court's ruling in *Lear* allowing the repudiating licensee to assert patent invalidity as a defense was entirely consistent with the traditional scope of licensee estoppel. The *Lear* Court did not perceive that consistency, however, because it assumed that licensee estoppel always had the broader scope granted in *Hazeltine* and in the lower court ruling in *Lear* itself. *See* 395 U.S. at 668. *Lear* even viewed cases in which the estoppel did not apply due to repudiation

or eviction as exceptions that undermined licensee estoppel, not reflections of its equitable scope. *Id.* at 667-68. Thus, the "general rule" of *Hazeltine* that *Lear* rejected, *id.* at 671, was not licensee estoppel in its historical equitable form.[19]

In the first decade after *Lear*, lower courts divided over how far its rationale extended. The Sixth Circuit, for example, reaffirmed the traditional rule of equity: a licensee may not raise an invalidity defense until it repudiates the license by stopping royalty payments and giving notice that it is challenging the patent's validity. *PPG Indus., Inc. v. Westwood Chem., Inc.*, 530 F.2d 700, 706 (6th Cir. 1976); *see also id.* at 707 (holding however that *termination* of license is not required to challenge validity). In sharp contrast, the Second Circuit upheld a validity challenge by a licensee while allowing the licensee to keep the benefit of the license. *Warner-Jenkinson Corp. v. Allied Chem. Corp.*, 567 F.2d 184 (2d Cir. 1977). But apart from *Warner-Jenkinson*, there appears to be no clear-cut precedent for an offensive suit by a licensee in the position of MedImmune here.[20]

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[19] *Lear* also misread several cases it relied on. For example, it described *Pope Manufacturing Co. v. Gormully*, 144 U.S. 224 (1892), as an early case rejecting licensee estoppel, *Lear*, 395 U.S. at 663-64 – a mischaracterization echoed by MedImmune, Pet'r Br. 34. In fact, *Pope* was a case of extreme overreaching involving a "unique . . . contract" imposing "unusual and oppressive" obligations, which purported to bar the licensee from challenging the validity of *unlicensed* patents even *after the license terminated*. 144 U.S. at 232-33, 237. Licensee estoppel as a rule of equity never would have applied on those facts.

[20] For example, MedImmune and the United States incorrectly cite *American Sterilizer Co. v. Sybron Corp.*, 526 F.2d 542 (3d Cir. 1975), as precedent for this suit; but in that case the licensee actually "refused to pay any royalties, thereby giving rise to th[e] action" and exposing itself to counterclaims asserted by the patentee. *Id.* at 544. The one other case MedImmune and the United States cite as precedent, *Precision Shooting Equipment Co. v. Allen*, 646 F.2d 313 (7th Cir. 1981), arguably provides more support for their position, but even there the licensee appears to have breached the license by stopping royalty payments *before* bringing

Even this modest confusion ended in 1982, when Congress consolidated all patent appeals in the Federal Circuit to "increase doctrinal stability in the field of patent law" and thereby spur innovation by giving greater certainty to patent rights. S. Rep. No. 97-275, at 5-6 (1981), *reprinted in* 1982 U.S.C.C.A.N. 11, at 15-16. From the outset, the Federal Circuit has indicated that the historical requirement of repudiation remains a precondition for validity challenges by licensees. *See* Rooklidge (Part II), 69 J. Pat. & Trademark Off. Soc'y at 19-21. And the Federal Circuit unequivocally reaffirmed that rule almost a decade ago – before the license between Genentech and MedImmune was entered into – by holding that licensee estoppel continues to apply until the licensee "(i) actually ceases payment of royalties, and (ii) provides notice to the licensor that the reason for ceasing payment of royalties is because it has deemed the relevant claims to be invalid." *Studiengesellschaft*, 112 F.3d at 1568.

Thus, with at most one or two scattered exceptions a quarter century ago, suits attacking patents by licensees in good standing have *never* been allowed in our judicial system – and certainly never by this Court. While MedImmune would have the Court believe that the Federal Circuit's decision in *Gen-Probe* was a radical departure from existing law, just the opposite is true: it is MedImmune's license-and-sue strategy that is essentially unprecedented.

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suit. *See Precision Shooting Equip. Inc. v. Holless W. Allen Inc.*, 492 F. Supp. 79, 86-87 (C.D. Ill. 1980), *aff'd*, 646 F.2d 313 (7th Cir. 1981). Admittedly, not all of the cases are clear. Much of the confusion – which MedImmune exploits – stems from the courts' post-*Lear* use of "repudiation" and "termination" interchangeably. *E.g.*, *PPG*, 530 F.2d at 707. Based on that purely semantic imprecision, *Warner-Jenkinson* even cited *PPG* as support for the novel holding that "repudiation of the licensing agreement should not be precondition to suit," 567 F.2d at 187, when in fact *PPG* held that breach plus notice to the patentee – repudiation in substance – was required, 530 F.2d at 706.

### C. Suits Like This Conflict with Fundamental Patent Policies.

#### 1. Retaining Repudiation as a Precondition of Suit Furthers the Core Purposes of Patent Law.

The question is thus whether the Court will upset settled understandings to allow licensees like MedImmune to lock in favorable license terms and sue at the same time, so that the licensee can keep the benefits of the license contract if it loses the lawsuit but escape its contractual obligation to pay royalties if it wins. Such "a major departure from the long tradition of equity practice should not be lightly" undertaken. *eBay*, 126 S. Ct. at 1839 (quotation marks omitted).

MedImmune (and the United States) argue that despite the unfairness of MedImmune's strategy, it should be allowed in furtherance of the "patent policy" of eliminating invalid patents. That blinkered approach fails even to acknowledge the fundamental purpose of patent law: to "promote the Progress of Science and useful Arts, by securing for limited Times to . . . Inventors the exclusive Right to their respective . . . Discoveries." U.S. Const. art. I, § 8, cl. 8; *see also, e.g.*, *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146 (1989). Nor does it mention the strong public interest in the efficient exploitation of technology through licensing arrangements, which "increase the value of intellectual property to consumers and to the developers of the technology." U.S. Dep't of Justice & Fed. Trade Comm'n, *Antitrust Guidelines for the Licensing of Intellectual Property* 5 (1995) ("*DOJ/FTC Licensing Guidelines*"). While the interest in eliminating invalid patents is not insubstantial, it must be balanced against these competing and fundamental purposes of patent law. *E.g., Dawson Chem. Co. v. Rohm & Haas Co.*, 448 U.S. 176, 221 (1980) (rejecting argument that policy of free competition

trumps "the policy of stimulating invention that underlies the entire patent system").

It is true that *Lear* itself failed even to mention the importance of incentives for invention and disclosure provided by our patent and licensing system, and instead treated elimination of invalid patents as the sole policy to be considered. But that one-sidedness was a defect in *Lear* that later decisions like *Dawson* and *Bonito Boats* rejected. *Lear* stands near the high-water mark of judicial suspicion of patents and patent licensing, which was also manifested in the Court's creation of expansive patent misuse doctrines based on antitrust concepts that have since been discredited – but that *Lear* relied on. 395 U.S. at 663, 666-67. After *Lear*, Congress rolled back the extravagant patent misuse theories of that era. 35 U.S.C. § 271(d) (providing that various licensing practices are not patent misuse in absence of market power); *see also Dawson*, 448 U.S. at 213; *Ill. Tool Works Inc. v. Indep. Ink, Inc.*, 126 S. Ct. 1281, 1290 (2006).

Rules that promote efficient licensing for technology transfer are critical for furthering fundamental patent goals. As the United States acknowledges, "patent licensing in general should be encouraged because it allows the efficient exploitation of technology and promotes competition and innovation." U.S. Br. 23-24; *see id.* at 2 ("intellectual property licensing can enhance consumer welfare by allowing for the efficient exploitation of intellectual property"); *DOJ/FTC Licensing Guidelines*, at 5 (licensing "can lead to more efficient exploitation of the intellectual property, benefiting consumers through the reduction of costs and the introduction of new products"). This Court, too, recently observed with approval that "some patent holders, such as university researchers or self-made inventors, might reasonably prefer to license their patents, rather than undertake efforts to secure the financing necessary to bring their works to market themselves." *eBay*, 126 S. Ct. at 1840.

Congress has strongly endorsed patent licensing. In addition to legislatively overruling decisions from the *Lear* era that proscribed licensing practices as patent misuse, 35 U.S.C. § 271(d)(1), (2), (4), in 1980 Congress enacted the Bayh-Dole Act, 35 U.S.C. § 200 *et seq.*, to allow nonprofit organizations that receive federal research funds (like City of Hope) to obtain title to patents resulting from such research and to license them for commercial exploitation. Bayh-Dole declared it a "policy and objective of the Congress" to promote such licensing. *Id.* § 200. The ability to enter into efficient licensing relationships not only ensures that new technology is put to its highest and best use, but also substantially augments the incentive to engage in the research that leads to new technologies in the first place – the very *raison d'etre* of the patent system. Not surprisingly, the pro-licensing regime of the Bayh-Dole Act has led to a wide array of life-saving and life-enhancing products, including vaccines, cancer therapies, and glaucoma treatments. Council on Governmental Relations, *The Bayh-Dole Act: A Guide to the Law and Implementing Regulations* (1999), *available at* http://www.ucop.edu/ott/faculty/bayh.html.

MedImmune's rule would undermine these core patent objectives by creating perverse incentives for inefficient licensing or no licensing at all. The price of a license necessarily reflects a compromise based on the parties' assessment of the likely cost and outcome of an infringement suit that the license precludes, including whether defenses such as invalidity and unenforceability would be upheld and, when an *application* is being licensed, the likelihood that any patent will issue at all. Thus, "the more likely that a patent will be found invalid if litigated, the lower the royalties it can command in licensing negotiations. After all, licensing takes place in the shadow of litigation, with licensing rates determined by the relative bargaining power of the patent holder and potential licensees/alleged infringers." Carl

Shapiro, *Patent System Reform: Economic Analysis and Critique*, 19 Berkeley Tech. L.J. 1017, 1034 (2004); *see also, e.g.*, 1 Jay Dratler, Jr., *Licensing of Intellectual Property* § 4.02[3][b] (2006) (factor in setting royalty is "likelihood that the patent will be held valid if challenged in court").

On MedImmune's theory, however, the license would lock only the patentee into the compromise price. The licensee could, at any time, try to escape its obligation under the license to pay the compromise royalty by attacking the patent's validity, even as it maintains the protection of the license in the event its lawsuit fails. The license would also reverse the remedial scheme created by Congress by giving the licensee complete and unfettered control over the timing and venue for litigation while tying the patentee's hands. The license would protect only the licensee, not the patentee. The Federal Circuit rightly stressed "the inequity" of MedImmune's proposed rule "when the patent owner, having contracted away its right to sue, is in continuing risk of attack on the patent whenever and wherever the licensee chooses – for example, if the product achieves commercial success – while the licensee can preserve its license and royalty rate if the attack fails." Pet. App. 7a.

Under such a regime, patentees will be much more reluctant to enter into licenses with compromise royalty rates than they are now. Some patentees will forgo licensing altogether to preserve their right to bring infringement suits. After all, the downside risk to the patentee of suing for infringement would be exactly the same as the downside of entering into a license under MedImmune's proposal: "extremely expensive," "lengthy," and "disruptive patent litigation." U.S. Br. 26. But the upside to the patentee of preserving the right to sue for infringement would be much greater than under a license, because the patentee could seek the statutory relief provided by Congress for infringement (rather than the compromise royalty rate) and would also

retain significant control over the time and place of litigation. The result would be increased incentives to choose costly litigation over contractual compromise – since the compromise does not preclude the litigation anyway.

In other instances, patentees might still enter into licenses, but would demand a higher royalty rate to cover their increased risks. The United States admits as much by proposing that patentees could "require prospective licensees to purchase a fully paid-up license" to overcome their risk under MedImmune's proposal. U.S. Br. 29; *see also* Paul A. Ragusa & Samantha M. French, *To Pay or Not To Pay*, 7 Patent Strategy & Management 1, 8 (2006) (under MedImmune's proposed rule, patentees "may consider demanding security, e.g., in the form of an initial lump-sum payment, as a hedge to cover future uncertainty").[21] That simply confirms that the MedImmune rule would raise royalty rates and, ultimately, prices for consumers. Moreover, the United States' proposal of fully paid licenses is economically unrealistic in many industries, including biotechnology, where potential infringers seek the protection of a license before *beginning* costly development of "pipeline" products that may never be approved for marketing, much less achieve commercial success. *See* Pharm. Research & Mfrs. of Am., *Pharmaceutical Industry Profile 2005*, at 4-5 (2005) (describing drug development process), *available at* http://www.phrma.org/files/2005 IndustryReport.pdf. As a result, the prohibitive cost of a

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[21] The United States suggests that higher royalties would be necessary only when "a would-be licensee . . . makes clear that it disputes the validity or applicability of the patent." U.S. Br. 28. But that is obviously false. Licensees could always adopt the very strategy chosen by MedImmune here: conceal the intent to sue until after the favorable royalty rate is negotiated and the license is signed. Every patentee would potentially face that risk from every licensee and would demand higher royalties to offset it.

fully paid-up license would frequently cause prospective licensees to abandon programs using patented technology for developing important new products before they get off the ground. When it sought additional licenses for its "pipeline" products, MedImmune itself stressed that "Genentech's licensing policy with respect to the [Cabilly II] patent has the potential to be a significant factor in MedImmune's research and development strategies." J.A. 431. Thus, as the United States previously explained to the Court, "a rule of law effectively requiring payments in a lump sum . . . would reduce the incentive to invent." Br. for United States as Amicus Curiae, *Aronson v. Quick Point Pencil Co.*, 440 U.S. 257 (1978) (No. 77-1413), 1978 WL 207171, at *23.

Nor is there merit to the United States' blithe assertion that this serious disruption to innovation and technology transfer would affect only a subset of suspect patents. U.S. Br. 26 ("Many patents are clearly valid, and thus are unlikely to be challenged"). As every patent lawyer knows, a well-heeled litigant can amass prior art references or concoct other bases to challenge the validity of virtually *any* patent. With no downside risk to the licensee if it loses, such challenges will almost always be worth pursuing, regardless of merit, once "the product achieves commercial success," Pet. App. 7a, and the resulting royalties become substantial – exactly the situation here. Indeed, a commercial venture with enormous revenues like MedImmune may use a costly validity strike suit to bully nonprofit research institutions like City of Hope into one-sided settlements regardless of the suit's merit. *See* 126 Cong. Rec. 29890, 29896 (1980) (statement of Rep. Smith) ("Evidence shows that the high cost of defending a patent is sometimes used to blackmail the owner into permitting infringements or into selling out at greatly reduced price").

These distortions are not needed to "unmuzzle" licensees to challenge suspect patents. *Lear* and the traditional

licensee estoppel rule ensure that licensees are always free to repudiate their license obligations in order to challenge validity. The situation here is completely different from the posture of *Lear* coming out of the California Supreme Court, which ruled that a license contract could permanently bar a validity suit by prohibiting termination. *Supra* at 37. MedImmune is free at any time to launch its attack – if it repudiates first.[22] To be sure, by shifting some risk to the licensee, the precondition of repudiation might sometimes lead licensees not to file validity suits. But as just discussed, maintaining some downside risk for licensees is a salutary measure for preventing meritless strike suits in this posture. There is no reason why a license should impose all the risk of litigation on patentees, and none on licensees.

Moreover, under legislation enacted after *Lear*, any person can initiate an administrative reexamination proceeding ubject to substantive limitations imposed by Congress.[23] Congress created this new "system of administrative reexamination of patents" to "strengthen[] investor confidence in the certainty of patent rights," which Congress believed were undermined by the cost, duration, and uncertainty of patent validity litigation in court. H.R. Rep. No. 96-1307, Part I, at 3-4 (1980). MedImmune not

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[22] In addition, the license agreement here allows MedImmune to terminate at will without breach on six months' notice. J.A. 409 § 7.04.

[23] The most important limitation is that both *ex parte* and *inter partes* reexamination may only be based on "prior art consisting of patents or printed publications," not other grounds for contesting patentability. 35 U.S.C. § 301; *see id.* §§ 302, 311(a). An *ex parte* requester also does not have a right to judicial review of a decision upholding the patent. *Id.* § 306. And although an *inter partes* requester may seek judicial review (assuming Article III is satisfied), *id.* § 315(b), Congress declined to extend *inter partes* procedures to preexisting patents like Cabilly II. *See* Pub. L. No. 106-113, tit. IV, § 4608(a), 113 Stat. 1501, 1536, 1501A-572 (1999).

only can use this administrative procedure – it has done so. Pet'r. Br. 48 n.18.

MedImmune's right to repudiate (or terminate on six months' notice) also gives the lie to its suggestion that its rule is needed to allow licensees to escape from bad bargains when circumstances change after a license is signed.[24] MedImmune's conduct belies any notion that unforeseen developments have made the license undesirable to it. Just the opposite is true: MedImmune's entire strategy is to avoid repudiation so it can *keep* the license. *Lear* and the traditional rule of equity already give MedImmune the right to escape from the bargain it made by repudiating and then attacking the validity of Cabilly II. Alleged changed circumstances cannot justify the one-sided rule sought by MedImmune.[25]

### 2. The Serious Flaws in MedImmune's Proposal Cannot Be Eliminated by Contract Rules.

The United States effectively acknowledges that patent policy does not really favor MedImmune's rule, *i.e.*, does not "entitle a licensee both to challenge the licensed patent and to retain all the benefits of his license agreement." U.S. Br. 28. But the United States contends that the licensee should have

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[24] As a factual matter, there is no merit to MedImmune's repeated complaints that the issuance of the Cabilly II Patent was somehow unforeseen. The possibility that Genentech and City of Hope would receive such a patent was expressly contemplated by the parties when they included the Cabilly II Application in the license, precisely so that MedImmune could not be sued for infringement if Respondents prevailed in the interference and received the patent. *Supra* at 5.

[25] Similarly, that several related patents are covered by the license does not favor allowing a validity challenge to one of the patents without repudiation. MedImmune chose for its own convenience to license multiple patents as a comprehensive shield against infringement suits. J.A. 402. Moreover, when parties license multiple patents, repudiation as to one would not necessarily trigger termination of the license as to others.

its cake and eat it too unless "the agreement expressly provides otherwise." *Id.* That importation of contract principles here is neither logical nor realistic. If patent policy truly favored the MedImmune rule, the United States would not try to reassure the Court that parties can avoid it contractually (nor conspicuously assert that the Government's own patents would be exempt from the rule it espouses, U.S. Br. 23 n.11). Indeed, if patentees could contract around the rule, in the future they would insist on express license terms providing that an attack on the patent's validity is a material breach of the license, *i.e.*, a repudiation. That would merely return future generations of licenses to the historical estoppel rule that has always applied.

In the meantime, the United States' proposal would unleash massive uncertainty about licenses negotiated before the announcement of this new rule. The scope of licensee estoppel has never been determined by contract. *Supra* at 34-39; *Lear*, 395 U.S. at 673 ("The parties' contract . . . is no[t] controlling on this issue"). The United States' rule would thus spawn a wave of satellite litigation about whether the current generation of patent licenses expressly or impliedly provide that filing litigation like this is a material breach – a topic the parties never contemplated as a matter for negotiation – and whether such a provision is enforceable. *See* U.S. Br. 28 ("the enforceability of such provisions is an open question"). As the brief of *amicus* Licensing Executive Society in support of neither party emphasizes, both licensors and licensees need additional certainty here, not the pervasive uncertainty that would be caused by this new rule.

In any event, if the license terms were controlling, they would bar this suit. The license here provides that MedImmune must pay royalties so long as the patents "have neither expired nor been held invalid by a court or other body of competent jurisdiction from which no appeal has been or may be taken." J.A. 399. As this Court explained a century

ago in construing a nearly identical provision – a "wellknown and conventional one in licenses" – such "proviso[s] [are] inserted . . . on the assumption that a licensee . . . *is estopped to deny the validity of the patent* which he has been using, and to give him the benefit of litigation by or against third persons, notwithstanding that rule." *Harvey*, 196 U.S. at 317 (emphasis added). Hence, "[i]t would not be enough to say that the [licensee] thought the patent bad, and would like to have the court decide so now." *Id.* at 316. MedImmune's contractual obligation is thus to pay royalties until the patent expires or is invalidated by a final decision in third-party litigation. This is a suit to *evade* that contractual obligation. And *Studiengesellschaft* provides the background rule implicitly incorporated into the parties' understanding: MedImmune cannot attack the patent in order to evade its contractual obligations unless it first repudiates the contract.

### D. As a Matter of Constitutional Avoidance, the Court Should Affirm on These Prudential Grounds.

The Court can and should affirm on these prudential grounds. In the courts below, City of Hope and Genentech properly relied on binding Circuit precedent deciding the jurisdictional issue under Article III, and so had no occasion to press the argument that prudential considerations also bar the exercise of jurisdiction. But because the issue is jurisdictional – albeit prudential and discretionary – this Court may address it in the first instance, with or without deciding the Article III question. *Catholic Soc. Servs.*, 509 U.S. at 57 n.18 ("Even when a ripeness question in a particular case is prudential, we may raise it on our own motion, and cannot be bound by the wishes of the parties") (quotation marks omitted); *Elk Grove Unified Sch. Dist. v. Newdow*, 542 U.S. 1, 11-18 & n.8 (2004); *Steel Co.*, 523 U.S. at 100 n.3; *id.* at 115 (opinion of Stevens, J.). Indeed, in *Cardinal*, even after finding Article III satisfied, the Court

*sua sponte* decided a discretionary jurisdiction question that had not been addressed by the Federal Circuit or briefed by the parties. *See* 508 U.S. at 103-04 (opinion of Scalia, J.).

MedImmune itself has consistently argued that the scope of licensee estoppel after *Lear* is directly relevant to the question of jurisdiction. *E.g.*, Pet. App. 4a-5a; Pet'r Br. 34-38. MedImmune and the United States have also both briefed issues of "patent policy" relevant to the prudential jurisdiction question, not Article III. Pet'r Br. 38-50; U.S. Br. 23-30. The Federal Circuit, too, has made its views known. It has unequivocally stated that the judgment on review is compelled by equity. Pet. App. 7a; *Gen-Probe*, 359 F.3d at 1382. And its cases culminating in *Studiengesellschaft* unambiguously demonstrate its reaffirmation of the historical scope of licensee estoppel.

Most importantly, affirmance on this basis is favored by the doctrine of constitutional avoidance – "the deeply rooted commitment not to pass on questions of constitutionality unless adjudication of the constitutional issue is necessary." *Newdow*, 542 U.S. at 11 (quotation marks omitted). As set forth above, this Court has never held that there is a justiciable controversy supporting a DJA suit where, as here, neither party could sue for a traditional coercive remedy. The Court should not sail into those uncharted waters now, when MedImmune's suit is jurisdictionally barred by equity in any event.

## CONCLUSION

The judgment of the Court of Appeals should be affirmed.

Respectfully submitted,

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# STATUTORY ADDENDUM

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### U.S. Const. art. I, § 8, cl. 8

The Congress shall have Power . . . To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.

### U.S. Const. art. III, § 2, cl. 1

The judicial Power shall extend to all Cases, in Law and Equity, arising under this Constitution, the Laws of the United States, and Treaties made, or which shall be made, under their Authority;—to all Cases affecting Ambassadors, other public Ministers and Consuls;—to all Cases of admiralty and maritime Jurisdiction;—to Controversies to which the United States shall be a Party;—to Controversies between two or more States;—between a State and Citizens of another State;—between Citizens of different States;—between Citizens of the same State claiming Lands under Grants of different States, and between a State, or the Citizens thereof, and foreign States, Citizens or Subjects.

### 28 U.S.C. § 2201. Creation of remedy

(a) In a case of actual controversy within its jurisdiction, except with respect to Federal taxes other than actions brought under section 7428 of the Internal Revenue Code of 1986, a proceeding under section 505 or 1146 of title 11, or in any civil action involving an antidumping or countervailing duty proceeding regarding a class or kind of merchandise of a free trade area country (as defined in section 516A(f)(10) of the Tariff Act of 1930), as determined by the administering authority, any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested

party seeking such declaration, whether or not further relief is or could be sought. Any such declaration shall have the force and effect of a final judgment or decree and shall be reviewable as such.

(b) For limitations on actions brought with respect to drug patents see section 505 or 512 of the Federal Food, Drug, and Cosmetic Act.

**35 U.S.C. § 131. Examination of application**

The Director shall cause an examination to be made of the application and the alleged new invention; and if on such examination it appears that the applicant is entitled to a patent under the law, the Director shall issue a patent therefor.

**35 U.S.C. § 134. Appeal to the Board of Patent Appeals and Interferences**

(a) Patent applicant. An applicant for a patent, any of whose claims has been twice rejected, may appeal from the decision of the primary examiner to the Board of Patent Appeals and Interferences, having once paid the fee for such appeal.

(b) Patent owner. A patent owner in any reexamination proceeding may appeal from the final rejection of any claim by the primary examiner to the Board of Patent Appeals and Interferences, having once paid the fee for such appeal.

(c) Third-party. A third-party requester in an inter partes proceeding may appeal to the Board of Patent Appeals and Interferences from the final decision of the primary examiner favorable to the patentability of any original or proposed amended or new claim of a patent, having once paid the fee for such appeal.

**35 U.S.C. § 135. Interferences**

(a) Whenever an application is made for a patent which, in the opinion of the Director, would interfere with any pending application, or with any unexpired patent, an interference may be declared and the Director shall give notice of such declaration to the applicants, or applicant and patentee, as the case may be. The Board of Patent Appeals and Interferences shall determine questions of priority of the inventions and may determine questions of patentability. Any final decision, if adverse to the claim of an applicant, shall constitute the final refusal by the Patent and Trademark Office of the claims involved, and the Director may issue a patent to the applicant who is adjudged the prior inventor. A final judgment adverse to a patentee from which no appeal or other review has been or can be taken or had shall constitute cancellation of the claims involved in the patent, and notice of such cancellation shall be endorsed on copies of the patent distributed after such cancellation by the Patent and Trademark Office.

(b)(1) A claim which is the same as, or for the same or substantially the same subject matter as, a claim of an issued patent may not be made in any application unless such a claim is made prior to one year from the date on which the patent was granted.

(2) A claim which is the same as, or for the same or substantially the same subject matter as, a claim of an application published under section 122(b) of this title may be made in an application filed after the application is published only if the claim is made before 1 year after the date on which the application is published.

(c) Any agreement or understanding between parties to an interference, including any collateral agreements referred to

therein, made in connection with or in contemplation of the termination of the interference, shall be in writing and a true copy thereof filed in the Patent and Trademark Office before the termination of the interference as between the said parties to the agreement or understanding. If any party filing the same so requests, the copy shall be kept separate from the file of the interference, and made available only to Government agencies on written request, or to any person on a showing of good cause. Failure to file the copy of such agreement or understanding shall render permanently unenforceable such agreement or understanding and any patent of such parties involved in the interference or any patent subsequently issued on any application of such parties so involved. The Director may, however, on a showing of good cause for failure to file within the time prescribed, permit the filing of the agreement or understanding during the six-month period subsequent to the termination of the interference as between the parties to the agreement or understanding.

The Director shall give notice to the parties or their attorneys of record, a reasonable time prior to said termination, of the filing requirement of this section. If the Director gives such notice at a later time, irrespective of the right to file such agreement or understanding within the six-month period on a showing of good cause, the parties may file such agreement or understanding within sixty days of the receipt of such notice.

Any discretionary action of the Director under this subsection shall be reviewable under section 10 of the Administrative Procedure Act.

(d) Parties to a patent interference, within such time as may be specified by the Director by regulation, may determine such contest or any aspect thereof by arbitration. Such arbitration shall be governed by the provisions of title 9 to

the extent such title is not inconsistent with this section. The parties shall give notice of any arbitration award to the Director, and such award shall, as between the parties to the arbitration, be dispositive of the issues to which it relates. The arbitration award shall be unenforceable until such notice is given. Nothing in this subsection shall preclude the Director from determining patentability of the invention involved in the interference.

**35 U.S.C. § 141. Appeal to Court of Appeals for the Federal Circuit**

An applicant dissatisfied with the decision in an appeal to the Board of Patent Appeals and Interferences under section 134 of this title may appeal the decision to the United States Court of Appeals for the Federal Circuit. By filing such an appeal the applicant waives his or her right to proceed under section 145 of this title. A patent owner, or a third-party requester in an inter partes reexamination proceeding, who is in any reexamination proceeding dissatisfied with the final decision in an appeal to the Board of Patent Appeals and Interferences under section 134 may appeal the decision only to the United States Court of Appeals for the Federal Circuit. A party to an interference dissatisfied with the decision of the Board of Patent Appeals and Interferences on the interference may appeal the decision to the United States Court of Appeals for the Federal Circuit, but such appeal shall be dismissed if any adverse party to such interference, within twenty days after the appellant has filed notice of appeal in accordance with section 142 of this title, files notice with the Director that the party elects to have all further proceedings conducted as provided in section 146 of this title. If the appellant does not, within thirty days after the filing of such notice by the adverse party, file a civil action under section 146, the decision appealed from shall govern the further proceedings in the case.

**35 U.S.C. § 145. Civil action to obtain patent**

An applicant dissatisfied with the decision of the Board of Patent Appeals and Interferences in an appeal under section 134(a) of this title may, unless appeal has been taken to the United States Court of Appeals for the Federal Circuit, have remedy by civil action against the Director in the United States District Court for the District of Columbia if commenced within such time after such decision, not less than sixty days, as the Director appoints. The court may adjudge that such applicant is entitled to receive a patent for his invention, as specified in any of his claims involved in the decision of the Board of Patent Appeals and Interferences, as the facts in the case may appear and such adjudication shall authorize the Director to issue such patent on compliance with the requirements of law. All the expenses of the proceedings shall be paid by the applicant.

**35 U.S.C. § 146. Civil action in case of interference**

Any party to an interference dissatisfied with the decision of the Board of Patent Appeals and Interferences on the interference, may have remedy by civil action, if commenced within such time after such decision, not less than sixty days, as the Director appoints or as provided in section 141 of this title, unless he has appealed to the United States Court of Appeals for the Federal Circuit, and such appeal is pending or has been decided. In such suits the record in the Patent and Trademark Office shall be admitted on motion of either party upon the terms and conditions as to costs, expenses, and the further cross-examination of the witnesses as the court imposes, without prejudice to the right of the parties to take further testimony. The testimony and exhibits of the record in the Patent and Trademark Office when admitted shall have the same effect as if originally taken and produced in the suit.

Such suit may be instituted against the party in interest as shown by the records of the Patent and Trademark Office at the time of the decision complained of, but any party in interest may become a party to the action. If there be adverse parties residing in a plurality of districts not embraced within the same state, or an adverse party residing in a foreign country, the United States District Court for the District of Columbia shall have jurisdiction and may issue summons against the adverse parties directed to the marshal of any district in which any adverse party resides. Summons against adverse parties residing in foreign countries may be served by publication or otherwise as the court directs. The Director shall not be a necessary party but he shall be notified of the filing of the suit by the clerk of the court in which it is filed and shall have the right to intervene. Judgment of the court in favor of the right of an applicant to a patent shall authorize the Director to issue such patent on the filing in the Patent and Trademark Office of a certified copy of the judgment and on compliance with the requirements of law.

**35 U.S.C. § 271. Infringement of patent**

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

(b) Whoever actively induces infringement of a patent shall be liable as an infringer.

(c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the

same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.

(d) No patent owner otherwise entitled to relief for infringement or contributory infringement of a patent shall be denied relief or deemed guilty of misuse or illegal extension of the patent right by reason of his having done one or more of the following: (1) derived revenue from acts which if performed by another without his consent would constitute contributory infringement of the patent; (2) licensed or authorized another to perform acts which if performed without his consent would constitute contributory infringement of the patent; (3) sought to enforce his patent rights against infringement or contributory infringement; (4) refused to license or use any rights to the patent; or (5) conditioned the license of any rights to the patent or the sale of the patented product on the acquisition of a license to rights in another patent or purchase of a separate product, unless, in view of the circumstances, the patent owner has market power in the relevant market for the patent or patented product on which the license or sale is conditioned.

(e)(1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

(2) It shall be an act of infringement to submit—

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent, or

(B) an application under section 512 of such Act or under the Act of March 4, 1913 (21 U.S.C. 151-158) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques and which is claimed in a patent or the use of which is claimed in a patent, if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug or veterinary biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

(3) In any action for patent infringement brought under this section, no injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention under paragraph (1).

(4) For an act of infringement described in paragraph (2)—

(A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date

which is not earlier than the date of the expiration of the patent which has been infringed,

(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug or veterinary biological product, and

(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug or veterinary biological product.

The remedies prescribed by subparagraphs (A), (B), and (C) are the only remedies which may be granted by a court for an act of infringement described in paragraph (2), except that a court may award attorney fees under section 285.

(5) Where a person has filed an application described in paragraph (2) that includes a certification under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), and neither the owner of the patent that is the subject of the certification nor the holder of the approved application under subsection (b) of such section for the drug that is claimed by the patent or a use of which is claimed by the patent brought an action for infringement of such patent before the expiration of 45 days after the date on which the notice given under subsection (b)(3) or (j)(2)(B) of such section was received, the courts of the United States shall, to the extent consistent with the Constitution, have subject matter jurisdiction in any action brought by such person under

section 2201 of title 28 for a declaratory judgment that such patent is invalid or not infringed.

(f)(1) Whoever without authority supplies or causes to be supplied in or from the United States all or a substantial portion of the components of a patented invention, where such components are uncombined in whole or in part, in such manner as to actively induce the combination of such components outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(2) Whoever without authority supplies or causes to be supplied in or from the United States any component of a patented invention that is especially made or especially adapted for use in the invention and not a staple article or commodity of commerce suitable for substantial noninfringing use, where such component is uncombined in whole or in part, knowing that such component is so made or adapted and intending that such component will be combined outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent. In an action for infringement of a process patent, no remedy may be granted for infringement on account of the noncommercial use or retail sale of a product unless there is no adequate remedy under this title for infringement on account of the importation or other use, offer to sell, or sale of that product. A product which is made by a

patented process will, for purposes of this title, not be considered to be so made after—

(1) it is materially changed by subsequent processes; or

(2) it becomes a trivial and nonessential component of another product.

(h) As used in this section, the term "whoever" includes any State, any instrumentality of a State, and any officer or employee of a State or instrumentality of a State acting in his official capacity. Any State, and any such instrumentality, officer, or employee, shall be subject to the provisions of this title in the same manner and to the same extent as any nongovernmental entity.

(i) As used in this section, an "offer for sale" or an "offer to sell" by a person other than the patentee, or any designee of the patentee, is that in which the sale will occur before the expiration of the term of the patent.

**35 U.S.C. § 281. Remedy for infringement of patent**

A patentee shall have remedy by civil action for infringement of his patent.

**35 U.S.C. § 282. Presumption of validity; defenses**

A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. Notwithstanding the preceding sentence, if a claim to a composition of matter is held invalid and that claim was the basis of a determination of nonobviousness under section

103(b)(1), the process shall no longer be considered nonobvious solely on the basis of section 103(b)(1). The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.

The following shall be defenses in any action involving the validity or infringement of a patent and shall be pleaded:

(1) Noninfringement, absence of liability for infringement or unenforceability,

(2) Invalidity of the patent or any claim in suit on any ground specified in part II of this title as a condition for patentability,

(3) Invalidity of the patent or any claim in suit for failure to comply with any requirement of sections 112 or 251 of this title,

(4) Any other fact or act made a defense by this title.

In actions involving the validity or infringement of a patent the party asserting invalidity or noninfringement shall give notice in the pleadings or otherwise in writing to the adverse party at least thirty days before the trial, of the country, number, date, and name of the patentee of any patent, the title, date, and page numbers of any publication to be relied upon as anticipation of the patent in suit or, except in actions in the United States Court of Federal Claims, as showing the state of the art, and the name and address of any person who may be relied upon as the prior inventor or as having prior knowledge of or as having previously used or offered for sale the invention of the patent in suit. In the absence of such notice proof of the said matters may not be made at the trial except on such terms as the court requires. Invalidity of the extension of a patent term or any portion thereof under

section 154(b) or 156 of this title because of the material failure—

(1) by the applicant for the extension, or

(2) by the Director,

to comply with the requirements of such section shall be a defense in any action involving the infringement of a patent during the period of the extension of its term and shall be pleaded. A due diligence determination under section 156(d)(2) is not subject to review in such an action.

**35 U.S.C. § 283. Injunction**

The several courts having jurisdiction of cases under this title may grant injunctions in accordance with the principles of equity to prevent the violation of any right secured by patent, on such terms as the court deems reasonable.

**35 U.S.C. § 284. Damages**

Upon finding for the claimant the court shall award the claimant damages adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use made of the invention by the infringer, together with interest and costs as fixed by the court.

When the damages are not found by a jury, the court shall assess them. In either event the court may increase the damages up to three times the amount found or assessed. Increased damages under this paragraph shall not apply to provisional rights under section 154(d) of this title.

The court may receive expert testimony as an aid to the determination of damages or of what royalty would be reasonable under the circumstances.

**35 U.S.C. § 285. Attorney fees**

The court in exceptional cases may award reasonable attorney fees to the prevailing party.

**35 U.S.C. § 301. Citation of prior art**

Any person at any time may cite to the Office in writing prior art consisting of patents or printed publications which that person believes to have a bearing on the patentability of any claim of a particular patent. If the person explains in writing the pertinency and manner of applying such prior art to at least one claim of the patent, the citation of such prior art and the explanation thereof will become a part of the official file of the patent. At the written request of the person citing the prior art, his or her identity will be excluded from the patent file and kept confidential.

**35 U.S.C. § 302. Request for reexamination**

Any person at any time may file a request for reexamination by the Office of any claim of a patent on the basis of any prior art cited under the provisions of section 301 of this title. The request must be in writing and must be accompanied by payment of a reexamination fee established by the Director pursuant to the provisions of section 41 of this title. The request must set forth the pertinency and manner of applying cited prior art to every claim for which reexamination is requested. Unless the requesting person is the owner of the patent, the Director promptly will send a copy of the request to the owner of record of the patent.

**35 U.S.C. § 303. Determination of issue by Director**

(a) Within three months following the filing of a request for reexamination under the provisions of section 302 of this

title, the Director will determine whether a substantial new question of patentability affecting any claim of the patent concerned is raised by the request, with or without consideration of other patents or printed publications. On his own initiative, and any time, the Director may determine whether a substantial new question of patentability is raised by patents and publications discovered by him or cited under the provisions of section 301 of this title. The existence of a substantial new question of patentability is not precluded by the fact that a patent or printed publication was previously cited by or to the Office or considered by the Office.

(b) A record of the Director's determination under subsection (a) of this section will be placed in the official file of the patent, and a copy promptly will be given or mailed to the owner of record of the patent and to the person requesting reexamination, if any.

(c) A determination by the Director pursuant to subsection (a) of this section that no substantial new question of patentability has been raised will be final and nonappealable. Upon such a determination, the Director may refund a portion of the reexamination fee required under section 302 of this title.

**35 U.S.C. § 304. Reexamination order by Director**

If, in a determination made under the provisions of subsection 303(a) of this title, the Director finds that a substantial new question of patentability affecting any claim of a patent is raised, the determination will include an order for reexamination of the patent for resolution of the question. The patent owner will be given a reasonable period, not less than two months from the date a copy of the determination is given or mailed to him, within which he may file a statement on such question, including any amendment to his patent and

new claim or claims he may wish to propose, for consideration in the reexamination. If the patent owner files such a statement, he promptly will serve a copy of it on the person who has requested reexamination under the provisions of section 302 of this title. Within a period of two months from the date of service, that person may file and have considered in the reexamination a reply to any statement filed by the patent owner. That person promptly will serve on the patent owner a copy of any reply filed.

**35 U.S.C. § 305. Conduct of reexamination proceedings**

After the times for filing the statement and reply provided for by section 304 of this title have expired, reexamination will be conducted according to the procedures established for initial examination under the provisions of sections 132 and 133 of this title. In any reexamination proceeding under this chapter, the patent owner will be permitted to propose any amendment to his patent and a new claim or claims thereto, in order to distinguish the invention as claimed from the prior art cited under the provisions of section 301 of this title, or in response to a decision adverse to the patentability of a claim of a patent. No proposed amended or new claim enlarging the scope of a claim of the patent will be permitted in a reexamination proceeding under this chapter. All reexamination proceedings under this section, including any appeal to the Board of Patent Appeals and Interferences, will be conducted with special dispatch within the Office.

**35 U.S.C. § 306. Appeal**

The patent owner involved in a reexamination proceeding under this chapter may appeal under the provisions of section 134 of this title, and may seek court review under the provisions of sections 141 to 145 of this title, with respect to any decision adverse to the patentability of any original or proposed amended or new claim of the patent.

**35 U.S.C. § 307. Certificate of patentability, unpatentability, and claim cancellation**

(a) In a reexamination proceeding under this chapter, when the time for appeal has expired or any appeal proceeding has terminated, the Director will issue and publish a certificate canceling any claim of the patent finally determined to be unpatentable, confirming any claim of the patent determined to be patentable, and incorporating in the patent any proposed amended or new claim determined to be patentable.

(b) Any proposed amended or new claim determined to be patentable and incorporated into a patent following a reexamination proceeding will have the same effect as that specified in section 252 of this title for reissued patents on the right of any person who made, purchased, or used within the United States, or imported into the United States, anything patented by such proposed amended or new claim, or who made substantial preparation for the same, prior to issuance of a certificate under the provisions of subsection (a) of this section.

**35 U.S.C. § 311. Request for inter partes reexamination**

(a) In general.—Any third-party requester at any time may file a request for inter partes reexamination by the Office of a

patent on the basis of any prior art cited under the provisions of section 301.

(b) Requirements.—The request shall—

(1) be in writing, include the identity of the real party in interest, and be accompanied by payment of an inter partes reexamination fee established by the Director under section 41; and

(2) set forth the pertinency and manner of applying cited prior art to every claim for which reexamination is requested.

(c) Copy.—The Director promptly shall send a copy of the request to the owner of record of the patent.

**35 U.S.C. § 312. Determination of issue by Director**

(a) Reexamination.—Not later than 3 months after the filing of a request for inter partes reexamination under section 311, the Director shall determine whether a substantial new question of patentability affecting any claim of the patent concerned is raised by the request, with or without consideration of other patents or printed publications. The existence of a substantial new question of patentability is not precluded by the fact that a patent or printed publication was previously cited by or to the Office or considered by the Office.

(b) Record.—A record of the Director's determination under subsection (a) shall be placed in the official file of the patent, and a copy shall be promptly given or mailed to the owner of record of the patent and to the third-party requester.

(c) Final decision.—A determination by the Director under subsection (a) shall be final and non-appealable. Upon a

determination that no substantial new question of patentability has been raised, the Director may refund a portion of the inter partes reexamination fee required under section 311.

**35 U.S.C. § 313. Inter partes reexamination order by Director**

If, in a determination made under section 312(a), the Director finds that a substantial new question of patentability affecting a claim of a patent is raised, the determination shall include an order for inter partes reexamination of the patent for resolution of the question. The order may be accompanied by the initial action of the Patent and Trademark Office on the merits of the inter partes reexamination conducted in accordance with section 314.

**35 U.S.C. § 314. Conduct of inter partes reexamination proceedings**

(a) In general.—Except as otherwise provided in this section, reexamination shall be conducted according to the procedures established for initial examination under the provisions of sections 132 and 133. In any inter partes reexamination proceeding under this chapter, the patent owner shall be permitted to propose any amendment to the patent and a new claim or claims, except that no proposed amended or new claim enlarging the scope of the claims of the patent shall be permitted.

(b) Response.—(1) With the exception of the inter partes reexamination request, any document filed by either the patent owner or the third-party requester shall be served on the other party. In addition, the Office shall send to the third-party requester a copy of any communication sent by the

Office to the patent owner concerning the patent subject to the inter partes reexamination proceeding.

(2) Each time that the patent owner files a response to an action on the merits from the Patent and Trademark Office, the third-party requester shall have one opportunity to file written comments addressing issues raised by the action of the Office or the patent owner's response thereto, if those written comments are received by the Office within 30 days after the date of service of the patent owner's response.

[(3) Redesignated (2)]

(c) Special dispatch.—Unless otherwise provided by the Director for good cause, all inter partes reexamination proceedings under this section, including any appeal to the Board of Patent Appeals and Interferences, shall be conducted with special dispatch within the Office.

**35 U.S.C. § 315. Appeal**

(a) Patent owner.—The patent owner involved in an inter partes reexamination proceeding under this chapter—

(1) may appeal under the provisions of section 134 and may appeal under the provisions of sections 141 through 144, with respect to any decision adverse to the patentability of any original or proposed amended or new claim of the patent; and

(2) may be a party to any appeal taken by a third-party requester under subsection (b).

(b) Third-party requester.—A third-party requester—

(1) may appeal under the provisions of section 134, and may appeal under the provisions of sections 141 through 144,

with respect to any final decision favorable to the patentability of any original or proposed amended or new claim of the patent; and

(2) may, subject to subsection (c), be a party to any appeal taken by the patent owner under the provisions of section 134 or sections 141 through 144.

(c) Civil action.—A third-party requester whose request for an inter partes reexamination results in an order under section 313 is estopped from asserting at a later time, in any civil action arising in whole or in part under section 1338 of title 28, the invalidity of any claim finally determined to be valid and patentable on any ground which the third-party requester raised or could have raised during the inter partes reexamination proceedings. This subsection does not prevent the assertion of invalidity based on newly discovered prior art unavailable to the third-party requester and the Patent and Trademark Office at the time of the inter partes reexamination proceedings.

**35 U.S.C. § 316. Certificate of patentability, unpatentability, and claim cancellation**

(a) In general.—In an inter partes reexamination proceeding under this chapter, when the time for appeal has expired or any appeal proceeding has terminated, the Director shall issue and publish a certificate canceling any claim of the patent finally determined to be unpatentable, confirming any claim of the patent determined to be patentable, and incorporating in the patent any proposed amended or new claim determined to be patentable.

(b) Amended or new claim.—Any proposed amended or new claim determined to be patentable and incorporated into a patent following an inter partes reexamination proceeding

shall have the same effect as that specified in section 252 of this title for reissued patents on the right of any person who made, purchased, or used within the United States, or imported into the United States, anything patented by such proposed amended or new claim, or who made substantial preparation therefor, prior to issuance of a certificate under the provisions of subsection (a) of this section.

**35 U.S.C. § 317. Inter partes reexamination prohibited**

(a) Order for reexamination.—Notwithstanding any provision of this chapter, once an order for inter partes reexamination of a patent has been issued under section 313, neither the third-party requester nor its privies, may file a subsequent request for inter partes reexamination of the patent until an inter partes reexamination certificate is issued and published under section 316, unless authorized by the Director.

(b) Final decision.—Once a final decision has been entered against a party in a civil action arising in whole or in part under section 1338 of title 28, that the party has not sustained its burden of proving the invalidity of any patent claim in suit or if a final decision in an inter partes reexamination proceeding instituted by a third-party requester is favorable to the patentability of any original or proposed amended or new claim of the patent, then neither that party nor its privies may thereafter request an inter partes reexamination of any such patent claim on the basis of issues which that party or its privies raised or could have raised in such civil action or inter partes reexamination proceeding, and an inter partes reexamination requested by that party or its privies on the basis of such issues may not thereafter be maintained by the Office, notwithstanding any other provision of this chapter. This subsection does not prevent the assertion of invalidity based on newly discovered prior art unavailable to the third-

party requester and the Patent and Trademark Office at the time of the inter partes reexamination proceedings.

**35 U.S.C. § 318. Stay of litigation**

Once an order for inter partes reexamination of a patent has been issued under section 313, the patent owner may obtain a stay of any pending litigation which involves an issue of patentability of any claims of the patent which are the subject of the inter partes reexamination order, unless the court before which such litigation is pending determines that a stay would not serve the interests of justice.

Supreme Court, U.S.
FILED
JUL 26 2006
OFFICE OF THE CLERK

No. 05-608

IN THE
# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

v.

GENENTECH, INC., ET AL.,

*Respondents.*

ON WRIT OF CERTIORARI TO THE
UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

## BRIEF OF RESPONDENT GENENTECH, INC.

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## QUESTION PRESENTED

Whether the Federal Circuit properly dismissed a suit brought by a patent licensee seeking a declaratory judgment that the patent was invalid or unenforceable, when the licensee's voluntary decision to enter the license agreement compromises those legal issues between the parties and grants the licensee complete immunity from a patent infringement suit?

## LIST OF PARTIES

Petitioner MedImmune, Inc. was the only appellant in the Federal Circuit, and Genentech, Inc., City of Hope, and Celltech R&D, Ltd. were appellees. Celltech is not a respondent in this Court, because Petitioner did not seek review of the Federal Circuit's decision concerning this party.

## RULE 29.6 STATEMENT

Approximately 56% of the issued common stock of Respondent Genentech, Inc. is owned by Roche Holdings, Inc. Respondent Genentech, Inc. remains an independent, publicly traded company.

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## STATUTES INVOLVED

Relevant constitutional and statutory provisions are set out in the Addendum to this brief.

## STATEMENT OF THE CASE

For more than 300 years, the common law and this Court have held that a patent licensee cannot challenge the validity of the patent while retaining the benefits conferred by the license. *E.g.*, *Kinsman v. Parkhurst*, 59 U.S. 289, 292–93 (1856). That rule was premised on the historic understanding of a license as an instrument of compromise. The parties exchange their claims and defenses under the patent laws for the rights and obligations negotiated in the contract, unless and until that contract is repudiated.

MedImmune argues that the Declaratory Judgment Act transforms that settled law by giving it a right to seek judicial advice about the merits of defenses to the potential infringement suit it has already compromised, without giving up the benefits of that compromise. It wants such advice to decide whether to abandon the license and quit paying royalties. But a justiciable controversy requires a dispute about *legal rights*, not simply a legal question that is "concrete" and of practical interest to the parties. MedImmune's legal rights and obligations are now defined by the license, and there is no dispute about them at all. Nor is MedImmune entitled to seek judicial advice about the merits of a settled patent claim by contending that its fear of the potential consequences of an infringement suit render the license a product of "duress." What MedImmune calls "duress" is nothing more than the decision every potential infringer confronts when it decides whether to compromise the risks of patent litigation in exchange for the certainty afforded by a license. The uncontroverted facts establish that MedImmune chose to license Respondents' patent, voluntarily, for the ordinary purpose of managing a legal risk. If the consequences of such a choice are a cognizable legal injury, then every licensee could unilaterally declare a "controversy" about the validity of any patent at any time.

The Federal Circuit correctly recognized that there is no Article III controversy here, but regardless this case must be dismissed as an exercise of the equitable discretion to decline jurisdiction provided in the Declaratory Judgment Act. Indeed, the equitable doctrine of licensee estoppel has foreclosed claims like these for centuries. As the Federal Circuit emphasized, it is "inequit[able]" to subject a patent owner to the "continuing risk of attack on the patent whenever the licensee chooses" while "the licensee can preserve its license and royalty rate if the attack fails," and this record compels that conclusion. Pet. App. 7a.[1]

## FACTUAL BACKGROUND

**Respondents' Patents.** Respondents Genentech, Inc. and City of Hope secured U.S. Patent No. 6,331,415 B1 ("the Cabilly II Patent"), after they invested years of effort and enormous financial resources developing genetic technology to produce antibodies used in, among other things, the diagnosis and treatment of cancer and other diseases. J.A. 109 (Am. Compl. ¶ 21), 417, 485, 509. The Cabilly II Patent relates to processes for the production of antibodies by "coexpression" of immunoglobulin chains in a recombinant host cell (the "coexpression technology"). J.A. 509, 549–50. Genentech uses this technology in a number of its own products, including treatments for breast and colorectal cancer. It also licenses the technology to other companies.

Respondents filed a patent application relating to this technology in 1983, and U.S. Patent No. 4,861,567 ("the Cabilly I Patent") was issued in March 1989. J.A. 109 (Am. Compl. ¶ 21); J.A. 485. The Cabilly I Patent is not the patent in suit. It generally claimed processes for the production of chimeric (genetically engineered) antibodies, but it did not expressly claim the coexpression technology. J.A. 485–505. It expired in March 2006.

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[1] "Pet. App." refers to the Appendix to the Petition for a Writ of Certiorari; "J.A." refers to the Joint Appendix; and "C.A.J.A." refers to the Federal Circuit Joint Appendix.

The PTO did not issue the Cabilly II Patent to Respondents until 2001. J.A. 350–53, 509. The delay was attributable to resolution of a priority dispute between Genentech and a British company, Celltech R&D, Ltd. Pet. App. 2a–4a. Celltech and Respondents had independently developed coexpression technology within weeks of each other. J.A. 344–45. Although Genentech was first to file for U.S. patent protection on April 8, 1983 (J.A. 277, 350), Celltech claimed priority based on a British patent application filed two weeks earlier. J.A. 277–78, 344. Genentech learned of this in 1989 when the PTO issued Celltech a patent for the coexpression technology (the "Boss Patent"). J.A. 459, 484. Believing Respondents had invented the technology, Genentech thereafter challenged the Boss Patent's priority by provoking a PTO interference proceeding. J.A. 278, 345.[2] Seven-and-a-half years after the declaration of interference, the Board of Patent Appeals found that Respondents had not established an actual reduction to practice before the British priority date and granted priority to Celltech. Pet. App. 2a. Respondents contested this decision by filing a civil action in federal court, which resulted in a mediated and judicially endorsed consent decree in Respondents' favor. J.A. 276–80, 343–48.

Although MedImmune contended in its complaint that the consent decree was "collusive" and "fraudulent" (Pet. App. 9a; J.A. 105, 120, 123, 130 (Am. Compl. ¶¶ 10, 66, 76, 106)), the district court rejected that claim on summary judgment (J.A. 357–71), the Federal Circuit affirmed (Pet. App. 9a–17a), and MedImmune did not challenge those rulings in this Court. As the Federal Circuit explained, the district court actively encouraged the parties to settle based on the strength of new evidence supporting Genentech's claim of priority. Pet. App. 2a–3a.[3] The district court

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[2] An interference is a PTO proceeding to determine certain questions of patentability or priority of invention between two or more parties claiming the same invention. 37 C.F.R. § 41.200(a); 35 U.S.C. § 135(a).

[3] During the discovery phase of the district court litigation, Respondents

observed that the new evidence "certainly put [Celltech] on the defensive," and strongly urged the parties to "agree on a mediator" and to "put [their] full effort into it." C.A.J.A. 1666; J.A. 332–33; Pet. App. 3a. The mediation was conducted by a retired judge, and the district court reviewed and approved the settlement, which resulted in a consent judgment that "Genentech is entitled as a matter of law to priority over Celltech to the invention." J.A. 343–48; Pet. App. 3a. The PTO then independently examined Genentech's patent application in light of the district court's judgment, concluded that it met all of the requirements of patentability, and issued the Cabilly II Patent to Genentech on December 18, 2001. J.A. 352–53, 509–51; Pet. App. 3a–4a.

**Public Notice Of Respondents' Patent Claims.** In 1991, MedImmune began developing Synagis, a monoclonal antibody used to prevent respiratory syncytial virus ("RSV"). J.A. 104 (Am. Compl. ¶ 5); Pet. Br. 2. As the district court found, MedImmune "utilizes the monoclonal antibody production techniques covered by the patents at issue" to make Synagis. J.A. 349–50; *see* Pet. Br. 2–3. By the time its development was underway, MedImmune was on notice that its use of the coexpression technology to make Synagis would expose it to infringement liability to either Celltech or Genentech for many years into the future.

The Boss Patent expressly claimed the coexpression technology, and became public when issued in 1989. J.A. 459, 484. The public record also demonstrated that Genentech claimed priority to the same invention. On the day the PTO issued the Boss Patent, it also issued the Cabilly I patent to Genentech, which described the coexpression technology but did not expressly claim it. J.A. 485–505; J.A. 109 (Am. Compl. ¶ 24). To provoke the interference, Genentech followed the "permitted and

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discovered a draft of the Cabilly patent application predating Celltech's British priority date and offered testimony from the attorney who drafted that application corroborating conception of the coexpression technology prior to March 25, 1983. J.A. 281–329; C.A.J.A. 1227–57. The parties supplemented the PTO record under 35 U.S.C. § 146. Pet. App. 9a.

standard procedure" of "copy[ing] exactly the claim[s] in Celltech's patent" into a pending continuation application that claimed the benefit of Genentech's 1983 application (the "Cabilly continuation application").[4] When the PTO declared an interference proceeding on February 28, 1991, it issued a public Notice of Declaration of Interference that disclosed that Genentech was asserting priority to the same coexpression technology claimed by the Boss Patent. J.A. 351, 459; 37 C.F.R. § 1.11(a) (1990); Notice of Declaration of Interference, Feb. 28, 1991, *available in* Patent No. 4,816,397 File History, Paper No. 25, at 4 (Cabilly continuation application claims Boss Patent claims 1–18). It was also a straightforward matter of law that Genentech would be entitled to protection for 17 years from the new patent's issuance if it established priority. 35 U.S.C. § 154(a)(2) (1994). As the Federal Circuit noted, PTO delays in the resolution of priority are "notorious." Pet. App. 11a.

**MedImmune's Decision to License the Coexpression Technology.** In 1997 and 1998, MedImmune acted to eliminate its risk of infringement liability by obtaining licenses to use the coexpression technology for the production of Synagis from both Celltech and Genentech. MedImmune obtained a license from Celltech for the Boss Patent in 1998. J.A. 134 (Am. Compl. ¶ 122). But in 1997 it also elected to secure protection from the known risk that Genentech could prevail in the then-pending interference proceeding by securing a license ("the 1997 License") not only to the Cabilly I Patent (relating to the production of chimeric antibodies), but also to any future patents "relating to the coexpression of immunoglobulin chains in recombinant host cells" (the "Coexpression Patents") that might issue from the Cabilly continuation application, pending at that time. J.A. 399 (Lic. ¶ 1.09). The terms of

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[4] J.A. 345, 351. The patent laws allow an application with new or amended claims—called a "continuation" or "continuing" application—to benefit from the filing date of an earlier application that discloses the claimed invention. *See* 35 U.S.C. §§ 120, 132(a); 37 C.F.R. § 1.121(c).

this license thus demonstrate MedImmune's awareness of the maximum scope of the patent rights Genentech might be granted if it prevailed in the priority dispute.[5] MedImmune was also necessarily agreeing that it desired the protection of the license notwithstanding that it might not know at the time of the license the precise claims of the patent that would ultimately issue. This was plainly a voluntary, uncoerced decision. MedImmune had no present need to license the coexpression technology from Genentech in 1997; Celltech owned the patent. MedImmune could have waited for the outcome of the interference proceeding, and concedes that it was given the option to license the chimeric and coexpression patents separately and was not "coerced" to take a package license. J.A. 402 (Lic. ¶ 2.04). Nonetheless, it chose to negotiate a comprehensive license with Genentech when Synagis was still in development and Genentech had only a prospect of obtaining a patent.

The resulting license terms reflected these advantageous bargaining conditions. The upfront payment was modest, J.A. 402, C.A.J.A. 3585 (Lic. ¶ 3.01), and the royalty rate was heavily discounted: slightly more than half the top rate that MedImmune later agreed to pay for additional licenses in 2003, *after* Genentech was awarded the Cabilly II patent. *Compare* J.A. 403, C.A.J.A. 3586 (Lic. ¶ 3.03) *with* J.A. 442, C.A.J.A. 3300 (Lic. ¶ 3.03). The 1997 License granted MedImmune "coexclusive" rights, which committed Genentech to granting no more than four additional licenses to practice in the same field and territory, a favorable term that MedImmune was unable to secure in subsequent non-exclusive licenses. *Compare* J.A. 401 (Lic. ¶ 2.01) *with* J.A. 441 (Lic. ¶ 2.01). It also contained a "Most Favored Licensee" provision that gave MedImmune the benefit of the best terms offered to any other party—

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[5] In any event, a prospective licensee who has any uncertainty about the scope of the claims covered by the application (and any amendments) can insist on reviewing those documents under a confidentiality agreement prior to executing a license. Licenses need not be taken blind.

another concession MedImmune was unable to secure in licenses negotiated after Cabilly II issued. J.A. 405 (Lic. ¶ 3.07). It also allowed MedImmune to "terminate [the license] in its entirety or with respect to one or more Antigens at any time upon six (6) months written notice." J.A. 409 (License ¶ 7.04).

MedImmune did not, however, negotiate any term that would permit it to initiate a judicial proceeding challenging the validity of the patents while retaining the benefits of the license. The 1997 License requires MedImmune to pay royalties unless and until the applicable patent is "held invalid by a court or other body of competent jurisdiction from which no appeal has been or may be taken." J.A. 399 (Lic. ¶ 1.10). That limitation is common in patent licenses, and this Court has held for 100 years that it does not give the licensee itself any contract right to challenge the validity of the patents; it simply gives the licensee "the benefit of litigation by or against third persons." *United States v. Harvey Steel Co.*, 196 U.S. 310, 317 (1905); *see also Blonder-Tongue Labs., Inc. v. Univ. of Ill. Found.*, 402 U.S. 313 (1971) (collateral estoppel produces the same result). Nothing in the license purported to alter the background rule—well-established by the time of the 1997 License—that unless the licensee repudiates the license it cannot avoid its royalty obligations by denying the patent's validity. *Studiengesellschaft Kohle m.b.H. v. Shell Oil Co.*, 112 F.3d 1561, 1568 (Fed. Cir.), *cert. denied*, 522 U.S. 996 (1997). Indeed, as MedImmune concedes, Genentech "disclaimed any warranty" as to the validity of any licensed patent. Pet. Br. 36 & n.15; J.A. 411 (Lic. ¶ 8.08).

**Petitioner's Decisions to Pay Royalties and Secure Additional Licenses.** Once the FDA approved Synagis in 1998 and MedImmune began making the product, MedImmune had to decide whether to make the royalty payments required by the licenses it negotiated, or instead repudiate or terminate those licenses. As MedImmune began to develop other products using the coexpression technology, it also had to decide whether to secure

additional licenses. The record leaves no doubt that the decisions MedImmune made with respect to these issues were wholly voluntary. It was not subjected to any pressure beyond its own assessment of the strength of Genentech's and Celltech's patent rights, clearly owed the royalties it elected to pay, and aggressively (and duplicitously) solicited seven new licenses from Genentech.

First, MedImmune elected to pay royalties under its license with Celltech. It did not deny that Synagis infringed the claims of the Boss Patent—the same claims found in the Cabilly II Patent.[6] J.A. 134 (Am. Compl. ¶ 124). This is all the more telling because Genentech requested that it also pay royalties to Genentech under the Cabilly I Patent, but MedImmune refused based on its view that "Synagis falls outside the claims of chimeric antibody patents." J.A. 414–16. (Genentech accepted that explanation and did not threaten suit or take any other adverse action.)

Three years later, in December 2001, the PTO issued the Cabilly II Patent. J.A. 509. Genentech contacted MedImmune in January 2002 "to confirm [its] expectation that MedImmune will pay royalties on sales of its Synagis antibody product." J.A. 419. MedImmune thus had to decide again whether to pay the royalties then due or instead repudiate or terminate the license. Desiring the benefits of its bargain but hoping to evade the price, MedImmune devised another way. As MedImmune would later testify, it decided to sue Genentech to challenge the validity of the patent, but not until it protected its downside by first inducing Genentech to grant it seven additional licenses under the Cabilly II Patent for various other antibody products then under development. J.A. 389, 431, 437. MedImmune began paying royalties under the Cabilly II Patent to maintain its commercial relationship with Genentech and its good standing under the 1997 License.

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[6] But for minor differences in dependent claims, the Cabilly II Patent contains claims identical to the Boss Patent. *Compare* J.A. 484 (claims 1–18 of the Boss Patent) *with* J.A. 550 (claims 1–20 of the Cabilly II Patent).

In the communications that followed the issuance of the Cabilly II Patent, MedImmune never once denied that it owed royalties under the license. J.A. 421–22, 426, 430–31, 434–35. Instead, it merely asked Genentech to explain its "basis for believing that [Synagis] would infringe any valid claim of the [Cabilly II] Patent such that royalties would be due," J.A. 421, and asserted that its March 2002 royalty payment had been made "under protest" while it was "evaluat[ing] [Genentech's] claim that MedImmune owes royalties." J.A. 426. By letter of March 24, 2002, Genentech responded to MedImmune's request and described why it believed that MedImmune was using the coexpression technology to produce Synagis. J.A. 428. The letter asked MedImmune to correct any misunderstanding Genentech had "regarding the structure of Synagis and/or the process by which it is produced." *Id.* MedImmune never responded, never challenged Genentech's understanding, and never offered any reason that royalties were not owed.

Instead, MedImmune continued paying quarterly royalties on Synagis (J.A. 108 (Am. Compl. ¶ 18)), and repeatedly communicated a desire to continue and expand its licensing relationship with Genentech. In a May 23, 2002 letter, for example, MedImmune stated that it was "happy to meet with [Genentech] to discuss whether Genentech is willing to license various MedImmune products in development on commercially reasonable terms." J.A. 434, 431. Genentech expressed "appreciat[ion for] MedImmune's interest in additional licenses under the [Cabilly II] patent" and stated that the company "look[ed] forward ... to continuing our commercial relationship." J.A. 429, 433. Based on these communications, and on MedImmune's silence following Genentech's explanatory letter of March 24, 2002, Genentech in good faith entered into negotiations with MedImmune. Those discussions culminated in agreements in January 2003 for seven new licenses to the Cabilly II Patent for MedImmune products in various stages of development. J.A. 439; J.A. 108 (Am. Compl. ¶ 18).

Then, just three months after it had secured the additional covenants not to sue, MedImmune filed this lawsuit challenging the validity and enforceability of the licensed patent. J.A. 1. MedImmune has since admitted that it had made the decision to file this challenge by March 2002. Pet. Br. 7; J.A. 389. It is plain as day why MedImmune waited a year to file and never disclosed its intentions to Genentech until after the new licenses were secured.[7]

## PROCEDURAL HISTORY

**Nature Of MedImmune's Claims.** MedImmune's claims warrant explanation because they bear on the jurisdictional issues. Its Amended Complaint alleged violations of antitrust and unfair competition laws that were dismissed on summary judgment and are no longer at issue. J.A. 141–48; Pet. App. 9a–17a. The remaining claims, as clarified during this litigation, seek a declaratory judgment that the Cabilly II patent is invalid and unenforceable *under the patent laws*. J.A. 115–30, 136–41.

Notwithstanding its inclusion of one cause of action for "Declaratory Judgment on Contractual Rights and Obligations," J.A. 136 (Am. Compl. ¶¶ 131–33), the supporting allegations of the complaint and MedImmune's explanations of its claims establish that MedImmune is not seeking a declaration of rights under the terms of the parties' contract. Its brief in this Court implies that there is a dispute under the contract because its obligation to pay royalties turns on whether Synagis "infringes one or more claims" of the patent, J.A. 399 (Lic. ¶ 1.10), and its complaint alleged "non-infringement." Pet. Br. 3–4; J.A. 108, 136, 141 (Am. Compl. ¶¶ 20, 132, 162–64). That is misleading. Its complaint alleges that Synagis does not infringe any "valid" claim of the patent. J.A. 141 (Am. Compl. ¶ 163). It never alleges that Synagis does not *in fact* utilize the technology

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[7] MedImmune has made a practice of negotiating licenses while intending to immediately challenge the licensed patent. *See MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376, 1377–78 (Fed. Cir. 2005), *petition for cert. filed*, 74 U.S.L.W. 3336 (U.S. Nov. 22, 2005) (No. 05-656).

claimed by the Cabilly II Patent. MedImmune's Federal Circuit brief explained its "non-infringement" argument in the following terms: "the Cabilly II claims cannot be supported by their limited specification and are invalid in light of prior art" and thus "unenforceable." Appellant's Br. at 2 (Fed. Cir. filed July 6, 2004). That is a challenge to the validity and enforceability of the Cabilly II Patent, not to whether Synagis infringes it according to the claims.

The courts below understood this. The district court found that Synagis *"utilizes the monoclonal antibody production techniques covered by the patents at issue."* J.A. 349–50 (Jan. 12, 2004 Memorandum of Decision) (emphasis added). The Federal Circuit also uniformly characterized MedImmune's claims as "challeng[ing] the validity and enforceability of the licensed patent." Pet. App. 1a; *see id.* at 4a, 6a–7a. Although MedImmune now suggests that the court of appeals should not have "assumed that Synagis was a 'Licensed Product,'" Pet. Br. 27, it did not contest the district court's finding or the Federal Circuit's characterization of its claims in its petition.[8]

MedImmune's alleged injuries are also relevant to the jurisdictional inquiry. First, MedImmune alleges that it has been "damaged" by the "payments to Genentech under the 1997 License Agreement based on sales of Synagis." J.A. 134–35 (Am. Compl. ¶ 125). Second, the complaint alleges that MedImmune "has, as a practical matter, been compelled—at great cost—to enter into the 2003 License Agreements with Genentech to protect its investments" in

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[8] The petition conspicuously asserted only that "the license for respondent's patent package included an application [the Cabilly continuation application] that, upon its issuance as [the Cabilly II Patent] and publication of its claims, petitioner believed to be invalid and unenforceable." Pet. 20. MedImmune's brief in this Court also admits that the Cabilly II Patent claims "the same technology that Celltech (through MRC) had once licensed to [it]," J.A. 134 (Am. Compl. ¶ 124), and therefore "purported to cover the process of producing *any* type of monoclonal antibody." Pet. Br. 4–5 (emphasis added). MedImmune describes Synagis as a "humanized monoclonal antibody." *Id.* at 3.

its pipeline products. J.A. 134 (Am. Compl. ¶ 125). In other words, MedImmune contends it is being injured by its own decisions to execute a license and pay royalties, in exchange for Genentech's covenant not to sue it for infringement.

**Proceedings In The District Court.** The district court dismissed the action. It first granted summary judgment to Genentech and Celltech on the antitrust and unfair-competition claims under the *Noerr-Pennington* doctrine, and rejected Petitioner's claim that the Cabilly II Patent was secured through fraud on the patent office. J.A. 349–79.

The district court dismissed the remaining declaratory judgment claims for lack of subject matter jurisdiction. Pet. App. 31a. The court found "no relevant facts that distinguish this case from" *Gen-Probe Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir.), *pet'n for cert. dismissed*, 543 U.S. 941 (2004), which held that there is no justiciable controversy over the validity of a patent between a patent holder and a licensee in good standing. Pet. App. 24a–31a.

**The Decision Of The Federal Circuit.** The Federal Circuit affirmed. It construed MedImmune's claims as a "challenge [to] the validity and enforceability of the licensed patent," Pet. App. 1a, and held that MedImmune "did not have standing" to bring claims that had been extinguished by the license. *Id.* at 9a. The panel reasoned that "[t]he Declaratory Judgment Act requires a 'definite and concrete controversy' of 'sufficient immediacy and reality,' to warrant judicial intervention," *id.* at 8a (quoting *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240 (1937), and *Md. Cas. Co. v. Pac. Coal & Oil Co.*, 312 U.S. 270, 273 (1941)), and that here "there is no controversy of immediacy or reality because there is no reasonable apprehension of suit." *Id.* It observed that here, as in *Gen-Probe* and *Centocor*, "the jurisdictional requirements of a declaratory action are not met when royalties are fully paid to the licensor and there is no ground on which the licensor can cancel the license or sue for infringement." *Id.* at 6a.

The Federal Circuit explained that its holding was compelled by "the equalizing principles that underlie the

Declaratory Judgment Act." *Id.* at 7a. "The purpose of [the declaratory judgment] procedure," the court noted, "is to 'accommodate[] the practical situation wherein the interest of one side to the dispute may be served by delay in taking legal action,' by permitting the other side to initiate legal action." *Id.* at 6a (quoting *BP Chems. Ltd. v. Union Carbide Corp.*, 4 F.3d 975, 977 (Fed. Cir. 1993)) (alteration in original). MedImmune's suit "distorts" that balance, and creates "inequity," by placing a patentee who has "contracted away its right to sue ... in continuing risk of attack on the patent whenever the licensee chooses—for example, if the product achieves commercial success—while the licensee can preserve its license and royalty rate if the attack fails." *Id.* at 7a. The Federal Circuit held that its decision was consistent with *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969), because in *Lear* "the licensee ceased payment and disavowed the license obligation," whereas MedImmune "assiduously avoided" breaching its license. Pet. App. 6a.

## SUMMARY OF ARGUMENT

I. This case is about what role a fully negotiated license plays in determining if a justiciable "case or controversy" exists between a licensee and licensor concerning the validity or enforceability of a patent. MedImmune and the United States claim that the license is "immaterial," U.S. Br. 21, but contracts often change the parties' relationship in a way that that brings their controversy to an end. The paradigmatic example is contracts settling an existing dispute, and courts routinely dismiss lawsuits as moot after settlements. A patent license is a contract in the nature of a settlement as well. It resolves a potential (or existing) statutory claim for patent infringement by redefining the parties' rights and obligations under the contract. As part of the bargain, the patent owner promises not to sue for infringement, thereby terminating any threat or uncertainty to the licensee deriving from the patent. Without more—and this case presents nothing more—the license is not only

material; it conclusively resolves any justiciable controversy concerning the patent between the parties to the license.

The Federal Circuit expressed this point through the "reasonable apprehension of suit" test developed in another context. That captures the right concept, because the impossibility of a statutory infringement suit precludes any controversy about the parties' respective legal rights under the patent laws. A fuller explanation is that justiciability has always been tied to an actual or imminent invasion of a legally protected interest, and, under basic legal principles going back 1500 years, voluntary payments to resolve uncertainty about one's legal rights do not constitute injury to any legally protected interest; rather, they terminate any controversy about those rights. Asserting that such payments are made "under protest" changes nothing. As this Court recognized in *Altvater v. Freeman*, it requires an "involuntary or coercive ... exaction," such as payments under an injunction, to establish that a royalty payment is an injury to a legally protected interest. 319 U.S. 359, 365 (1943). A compromise of uncertain legal rights is never legally "coerced" by the hazards and expense of litigation; otherwise, no settlement would ever be final.

Nor is MedImmune entitled to litigate the hypothetical question of what its legal rights *would* be *if* it renounced the license and continued selling Synagis. This Court has permitted litigants to challenge statutes or regulations without violating them, on the theory that the consequences of violation coerce the litigants into changing their primary conduct in ways that prevent any action based on actual prosecution from ripening. Equity was flexible enough to accommodate the necessity for early judicial intervention in appropriate circumstances, and Article III can be as well. But no such accommodation is appropriate in this case. MedImmune is not suffering any present injury *because it has voluntarily elected to purchase immunity from the potential cause of such an injury.* It voluntarily opted out of the statutory patent system with a license, and it is free to opt back in at any time by repudiating or terminating that

license. Its curiosity about the wisdom of doing so does not create a dispute about its legal rights. MedImmune is exactly like a party that settles a looming tort suit in exchange for a payment due in six months, and then comes to court for a declaration about the merits of that suit to decide whether to abandon its settlement.

Put another way, mootness, ripeness, and standing principles combine to render this case nonjusticiable. By taking a license, MedImmune mooted any prior controversy between itself and Genentech about their respective rights under the patent laws. It also severed any connection between its own legal rights and the validity of Genentech's patent that could create standing to litigate the validity issue. There is a potential *future* controversy about the validity of the patent, but that controversy will not ripen until MedImmune repudiates or terminates the license.

MedImmune argues at great length that because one purpose of the Declaratory Judgment Act was "to permit judicial resolution of contract disputes 'before or after breach,'" Pet. Br. 12–13 (citation omitted), the Federal Circuit erred by "announc[ing] an absolute rule that no 'actual controversy' can exist without breach of contract." *Id.* at 21. This is misdirection. There is no dispute about the meaning of the license or the parties' legal obligations under it, and the Federal Circuit did not hold that controversies about contract rights can never ripen prior to breach. This case is about whether MedImmune can litigate the merits of a hypothetical infringement suit that cannot arise because of the license—even though no dispute has arisen about the terms of that license—simply because the parties' *economic* interests are adverse and because a favorable decision would clear the way for MedImmune to abandon the contract. The Federal Circuit properly recognized that in these circumstances MedImmune "did not have standing to bring a declaratory challenge to the Cabilly II patent," Pet. App. 9a, because it faces no danger to any legally protected interest. The Declaratory Judgment Act might allow parties to seek clarification of their contractual obligations,

but it does not allow them to seek anticipatory judicial advice about how hypothetical legal rights *outside the contract* might be adjudicated if the contract did not exist.

Applying traditional Article III principles in this case will in no way "[c]onstitutionalize the rejected doctrine of licensee estoppel." Pet. Br. 34. This argument, ostensibly based on *Lear v. Adkins*, is in reality just a plea for a policy-based exception to the case or controversy requirement. *Lear* does not address justiciability and its substantive holding—that a licensee who has repudiated may assert invalidity as a defense to an infringement suit—applies only in circumstances where justiciability is obvious because the patent owner has filed suit or the putative infringer has reason to fear such a suit. This Court should not distort traditional Article III principles to promote MedImmune's particular (and deeply flawed) vision of sound patent policy.

II. This Court has explained that, regardless of whether the requirements of Article III are satisfied, declaratory judgment cases should be dismissed on jurisdictional grounds if it is clear that granting declaratory relief would be inconsistent with equitable principles. Permitting MedImmune to bring this suit while maintaining the down-side protection of its license is inconsistent with at least three centuries of equity jurisprudence directly on point (jurisprudence that was not, as MedImmune claims, rejected in *Lear v. Adkins*). Even leaving licensee estoppel aside, this suit violates fundamental norms of equity, including the principle that a party cannot continue taking the benefits of a contract while attacking it as voidable.

Nor does federal patent policy call for a departure from settled equitable rules. The goals of the patent system are greater than encouraging litigation. Creating incentives to innovation is the primary goal, and it is served by legal rules that promote predictable technology transfers. The new rule MedImmune seeks would encourage challenges to patents by licensees—but only at the expense of distorting market-based pricing and decreasing a license's value as a tool of compromise. That will lead to fewer licenses being

granted and therefore less innovation and less competition. The United States effectively concedes that these results are not required by public policy, by suggesting that licensors contract around them—either by requiring fully paid-up licenses or by inserting a clause making explicit that lawsuits like this one constitute breach. But if this case is just about picking the right contractual default rule then surely the answer is supplied by the common law, which has recognized for centuries that suits like this one are inconsistent with the bargain at the heart of a license.

## ARGUMENT

### I. THERE IS NO "ACTUAL CONTROVERSY"

MedImmune contends that it is entitled to litigate the merits of a hypothetical patent infringement suit, simply because a favorable decision would give it the confidence to stop purchasing insurance against that lawsuit. But a justiciable controversy requires some injury or threat to legal rights. MedImmune's decision to purchase immunity from suit terminates any controversy about the merits of that suit unless, as in *Altvater*, MedImmune can show that that decision was involuntary or coerced. It clearly cannot.

#### A. A Justiciable Controversy Requires An Actual Or Imminent Legal Injury, Or A Real Necessity For Anticipatory Judicial Action

This case requires careful attention to the constitutional limits on anticipatory or hypothetical adjudication. MedImmune quotes *Aetna* for the proposition that a declaratory judgment controversy must be "concrete" and not "hypothetical," and must "admit[] of an immediate and definitive determination of the legal rights of the parties," 300 U.S. at 240–41, but then argues as if these phrases come from nowhere—and as if "the legal rights of the parties" embraces any legal question of practical interest to them. *See* Pet. Br. 15. In fact the common law and this Court's standing and ripeness cases lay out a cohesive jurisprudence of when a justiciable controversy can exist prior to an actual violation of legal rights. That jurisprudence *does not* permit

federal courts to opine on any legal question that the parties care about and can state in concrete terms.

First, the controversy must concern the legal rights of the parties. Like any patent licensee, MedImmune would benefit from the declaration it seeks in a practical way, because if the patent were declared invalid it could stop paying royalties. But a federal court may not decide a dispute simply because the plaintiff will benefit from a favorable decision. That much "might be said of someone who has placed a wager upon the outcome." *Vermont Agency of Natural Res. v. United States ex rel. Stevens*, 529 U.S. 765, 772 (2000). The party's interest must "consist of obtaining compensation for, or preventing, the violation of a legally protected right." *Id.* MedImmune and its amici misread *Aetna* and *Maryland Casualty* by arguing that Article III requires only a factually concrete dispute with some practical consequence for the parties. *See, e.g.*, Pet. Br. 25; U.S. Br. 10; NRDC Br. 6. As *Aetna* put it, the controversy must be "definite and concrete" but must also "touch[] the legal relations of parties having adverse *legal interests*" and "admit[] of an immediate and definitive determination of the *legal rights* of the parties." 300 U.S. at 240–41 (emphasis added). Similarly, the Declaratory Judgment Act is limited to declarations about "rights and other legal relations." 28 U.S.C. § 2201(a).

Stated differently, in order to establish standing and the existence of a *legal* controversy the plaintiff always bears the burden[9] of tying whatever injury it claims to be suffering to some invasion (or threatened invasion) of an interest protected by common law, statute, or the Constitution.[10] "The alleged injury must be legally and

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[9] *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 95 (1993) ("[A] party seeking a declaratory judgment has the burden of establishing the existence of an actual case or controversy."); *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 561 (1992) (standing is "part of the plaintiff's case" and "must be supported in the same way as any other matter on which the plaintiff bears the burden of proof").

[10] *See, e.g., Warth v. Seldin*, 422 U.S. 490, 500 (1975) ("Although standing

judicially cognizable," *Raines v. Byrd*, 521 U.S. 811, 819 (1997), which does not require that the claim be *meritorious* but does mean that "[t]he injury must be to the sort of interest that the law protects when it is *wrongfully* invaded," *Aurora Loan Servs. v. Craddieth*, 442 F.3d 1018, 1024 (7th Cir. 2006) (Posner, J.).[11] The case then becomes moot if circumstances change such that "the parties lack a legally cognizable interest in the outcome," even if it remains important to them in some practical sense. *Powell v. McCormack*, 395 U.S. 486, 496 (1969); *County of Los Angeles v. Davis*, 440 U.S. 625, 631 (1979) (case is moot when "neither party has a legally cognizable interest in the final determination of the underlying questions of fact and law").

Second, in the absence of some special justification an injury to legally protected interests must already have occurred, or at least must be "imminent" or "certainly impending." *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 564 n.2 (1992); *see also Whitmore v. Arkansas*, 495 U.S. 149,

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in no way depends on the merits of the plaintiff's contention that particular conduct is illegal, it often turns on the nature and source of the claim asserted.") (citation omitted); *Flast v. Cohen*, 392 U.S. 83, 102 (1968) ("[I]n ruling on standing, it is both appropriate and necessary to look to the substantive issues ... to determine whether there is a logical nexus between the status asserted and the claim sought to be adjudicated."); *McConnell v. FEC*, 540 U.S. 93, 227 (2003) ("[T]o satisfy our standing requirements, a plaintiff's alleged injury must be an invasion of a concrete and particularized legally protected interest."); *Int'l Primate Protection League v. Adm'rs of Tulane Educ. Fund*, 500 U.S. 72, 77 (1991) ("[S]tanding is gauged by the specific common-law, statutory, or constitutional claims that a party presents."); William A. Fletcher, *The Structure of Standing*, 98 Yale L.J. 221, 229 (1988) ("The essence of a true standing question is the following: Does the plaintiff have a legal right to judicial enforcement of an asserted legal duty? This question should be seen as a question of substantive law, answerable by reference to the statutory or constitutional provision whose protection is invoked.").

[11] Ordinarily the litigant must claim an injury to *his own* legal rights, although in some instances it may be permitted to complain about what would ordinarily be regarded as a violation of the legal rights of a third party. "In such instances, the Court has found, in effect, that the constitutional or statutory provision in question implies a right of action in the plaintiff." *Warth*, 422 U.S. at 501.

158 (1990) ("Each of these cases demonstrates what we have said many times before and reiterate today: Allegations of possible future injury do not satisfy the requirements of Art. III. A threatened injury must be 'certainly impending' to constitute injury in fact.") (citations omitted). That rule essentially tracks the traditional common law requirements for relief at law or in equity, which is not surprising or accidental. Justiciability at common law was defined by the system of writs; the "jurisdictional" question was whether the plaintiff had averred sufficient facts to show that it was entitled to relief under the particular writ it asserted.[12] And the "case or controversy" limitation was designed, in part, to confine the federal courts to disputes "of the sort traditionally amenable to, and resolved by, the judicial process." *Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 102 (1998); *see also, e.g., Joint Anti-Fascist Refugee Comm. v. McGrath*, 341 U.S. 123, 150 (1951) (Frankfurter, J., concurring) (disputes "consonant with what was, generally speaking, the business of the Colonial courts and the courts of Westminster when the Constitution was framed"); *Vt. Agency*, 529 U.S. at 774.

The vast majority of declaratory judgment cases easily satisfy the requirement of an actual or imminent injury to legally protected rights. In "alternative relief" cases, for example, the declaratory judgment plaintiff has suffered an actionable injury and has a ripe cause of action for damages or an injunction, but instead chooses to seek a declaration. *See, e.g., Nashville, Chattanooga & St. Louis Ry. Co. v. Wallace*, 288 U.S. 249, 263 (1933) ("While the ordinary course of judicial procedure results in a judgment requiring

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[12] *See, e.g.*, Joseph Vining, *Legal Identity: The Coming of Age of Public Law* 55 (1978) ("Courts, whose jurisdiction was defined by the system of writs, did not need to speak of standing. The question was whether a challenger was entitled to a writ, whether he had a cause of action, whether the writ lay."); Fleming James, Jr., *Civil Procedure* § 1.3 (1965) (standing in king's court determined by whether plaintiff had proved a case in a particular cause of action); Theodore F. T. Plucknett, *A Concise History of the Common Law* 354 (5th ed. 1956).

an award of process or execution to carry it into effect, such relief is not an indispensable adjunct to the exercise of the judicial function."). In a "mirror image" suit like *Aetna*, the *other* party has suffered a legally cognizable injury but has not yet filed a lawsuit—and the likely defendant seeks a declaration in order to resolve the uncertainty. *See Aetna*, 300 U.S. at 244. As this Court stressed in both *Aetna* and *Maryland Casualty*, declaratory relief is permitted in these cases because "[i]t is the nature of the controversy, not the method of its presentation or the particular party who presents it, that is determinative." *Id.*; *Md. Cas.*, 312 U.S. at 273 ("It is immaterial that frequently, in the declaratory judgment suit, the positions of the parties in the conventional suit are reversed; the inquiry is the same in either case.").[13] The key point in both the "alternative relief" and "mirror image" situations is that the existence of a ripe traditional cause of action between the parties makes it clear that a justiciable "controversy" exists.

It is "anticipatory" cases, where a party seeks a declaration prior to the point at which a cognizable injury has been suffered or is "imminent," that push the outer boundary of the case or controversy limitation. Such cases threaten to bring into court disputes that would never have been ripe prior to the Declaratory Judgment Act, in conflict with this Court's repeated assurance that the Act is "procedural" and does not expand the jurisdiction of the federal courts. *See, e.g., Aetna*, 300 U.S. at 240. Both the common law and this Court have authorized judicial intervention before the feared injury to legally protected interests is "imminent" or "certainly impending," but only in limited circumstances and with very special justification.

The common law recognized a limited, and sparingly applied, category of equitable relief known as bills *quia*

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[13] Although under state procedure, the tort plaintiff in *Maryland Cas.* may have been unable to sue the insurer prior to obtaining a judgment against the insured, under *federal* procedure either party could have joined the insurance company to avoid the risk of inconsistent judgments.

*timet* ("because he fears"), which were "ordinarily applied to prevent wrongs or anticipated mischiefs, and not merely to redress them when done."[14] An individual could, for example, bring a *quia timet* suit at common law claiming that its future property interests were in danger of being diverted or squandered, and courts had discretion to appoint a receiver or to require security in order to protect the plaintiff's future property rights. The test was that the threatened injury must either be "so imminent that no one can doubt that, if the remedy is delayed, the damage will be suffered" or "it must be shown that ... it will be impossible for the plaintiff to protect himself against [injury] if relief is denied to him in a *quia timet* action." *Fletcher v. Bealey*, 28 Ch.D. 688, 698 (1885). Legal uncertainty alone was never enough.[15] This Court has recognized that a request "for an adjudication of rights in anticipation of their threatened infringement" under the Declaratory Judgment Act is constitutionally justified in part by "analog[y] to the equity jurisdiction in suits *quia timet* or for a decree quieting title." *Great Lakes Dredge & Dock Co. v. Huffman*, 319 U.S. 293, 300 (1943); *see also, e.g., Am. Auto. Ins. Co. v. Freundt*, 103 F.2d 613, 617 (7th Cir. 1939) ("The roots of the declaratory

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[14] 2 Joseph Story, *Commentaries on Equity Jurisprudence: As Administered in England and America* 156–57 (1886); *see also, e.g.*, 27A Am. Jur. 2d Equity § 93 (1996); *City of New Orleans v. Christmas*, 131 U.S. 191, 212 (1889) ("'A court of equity will also prevent injury in some cases by interposing before any actual injury has been suffered, by a bill which has sometimes been called a bill *quia timet* ....'") (citation omitted); *Flight v. Cook*, 2 Ves. Sen. 619, 619–20 (Eng. Ch. 1755) (*quia timet* relief should be cautiously invoked).

[15] *See, e.g., Willing v. Chicago Auditorium Ass'n*, 277 U.S. 274, 289–90 (1928) (There is no action in equity to remove "plaintiff's ... own doubts," where "[n]o defendant has wronged the plaintiff or has threatened to do so." Such an action "was unknown to either English or American courts at the time of the adoption of the Constitution and for more than a half a century thereafter."); *Edison Elec. Light Co. v. Kaelber*, 76 F. 804, 806 (C.C.N.D.N.Y. 1896) ("A *quia timet* action will not lie unless there is something to fear.").

judgment procedure are found in equity procedure, chiefly in the *quia timet* relief.").

Both the common law and this Court have also permitted litigants to challenge official action believed to be contrary to law, without necessarily exposing themselves to the risk of enforcement. *See, e.g., Ex Parte Young*, 209 U.S. 123 (1908); *Steffel v. Thompson*, 415 U.S. 452 (1974); *Abbott Labs. v. Gardner*, 387 U.S. 136 (1967), *overruled on other grounds by Califano v. Sanders*, 430 U.S. 99, 107 (1977). Such pre-enforcement review is justified if the litigant is being "coerced" to alter its primary conduct by the threat of enforcement. As the treatise this Court cited in *Altvater* makes clear, the common law regarded threats under color of official authority as inherently coercive. *See* Frederic Campbell Woodward, *The Law of Quasi Contracts* 348 (1913) ("[I]n the case of a refusal by a public officer to perform a duty, the courts, recognizing the inherent advantage of his position and the importance of protecting those who deal with him, require no additional evidence that the act is coercive."). In *Steffel*, for example, this Court observed that refusing pre-enforcement review of a criminal statute would "place the hapless plaintiff between the Scylla of intentionally flouting state law and the Charybdis of forgoing what he believes to be constitutionally protected activity in order to avoid becoming enmeshed in a criminal proceeding." 415 U.S. at 462. On the other hand, "a justiciable controversy does not exist where 'compliance with [challenged] statutes is uncoerced by the risk of their enforcement.'" *Lake Carriers' Ass'n v. MacMullan*, 406 U.S. 498, 507 (1972) (citation omitted). Absent a real threat of enforcement, there is no coercion and no necessity for judicial intervention before a litigant's legally protected interests are invaded.[16]

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[16] City of Hope shows that cases like *Steffel* and *Ex Parte Young* might also be read as involving fully realized injury to a distinct legal right (a right to be free from threats of unlawful action by state officials that compel abandonment of constitutionally protected rights), such that

The common thread in all of these cases is that a litigant cannot claim a justiciable "controversy" over a potential future injury *that the litigant itself is preventing* unless the law is prepared to regard that preventive behavior as involuntary or coerced. The common law *quia timet* cases captured that concept by saying that anticipatory relief was generally unavailable if it was possible "for the Plaintiff to protect himself against [the harm]." *Fletcher*, 28 Ch.D. at 698. This Court explained in *Lujan* that the constitutional requirement of an "imminent" injury is "stretched beyond the breaking point" when "the plaintiff alleges only an injury at some indefinite future time, and the acts necessary to make the injury happen are at least partially within the plaintiff's own control." *Lujan*, 504 U.S. at 564 n.2. If the plaintiff itself can prevent any injury from occurring, without surrendering its legal rights, then that injury is ordinarily neither sufficiently "imminent" nor "'fairly ... trace[able] to the challenged action of the defendant.'" *Id.* at 560 (citations omitted) (alterations in original). Or, in the language of this Court's ripeness cases, there is not sufficient "hardship to the parties of withholding court consideration" to justify anticipatory relief. *Abbott Labs.*, 387 U.S. at 149. Considerations of hardship and necessity have similarly justified exceptions from ordinary mootness principles when the mootness is beyond the litigant's control (such as when injuries are capable of repetition yet evading review), but this Court has made it clear that *voluntary* action mooting a case destroys the controversy and renders it non-justiciable. *U.S. Bancorp Mortgage Corp. v. Bonner Mall P'ship*, 513 U.S. 18, 25 (1994) ("Where mootness results from settlement, ... the losing party has voluntarily

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they do not involve or justify "anticipatory" declaratory relief. In contrast to the reading above, that would foreclose adjudication of truly anticipatory cases (such as suits to interpret a contract prior to actual or imminent breach, or to test the scope or validity of a patent prior to actual or imminent infringement). *Compare supra* at 21–23 *with* Resp. City of Hope Br. 19–22. This Court need not choose between these readings here because this suit is non-justiciable under either view.

forfeited his legal remedy by the ordinary processes of appeal or certiorari, thereby surrendering his claim to the equitable remedy of vacatur.").[17]

MedImmune is therefore wrong to suggest that Article III is satisfied simply by a disagreement over a point of law that the parties care about, and that is factually concrete enough to permit a definite answer. MedImmune must identify some injury *to legal rights or legally protected interests*, and it must show that the alleged injury has occurred, is "imminent" or "certainly impending," or otherwise presents a compelling necessity for review prior to the point at which judicial intervention has traditionally been available. If the injury it claims to fear will likely never occur because of uncoerced choices MedImmune is making, then there is no justiciable controversy.

### B. There Is No Cognizable Injury Or Coercion Creating A Justiciable Controversy In This Case

#### 1. Voluntary Royalty Payments Are Not An Injury To MedImmune's Legal Rights

MedImmune bears the burden of tying the injury it claims to be suffering to the violation of some alleged legal right or legally protected interest. To the extent MedImmune addresses that central question at all, it simply assumes that paying royalties on a patent it believes to be invalid is a violation of its legal rights. But MedImmune utterly fails to identify any statutory or other source for such a right—because no right exists. MedImmune's assumption is inconsistent with a basic legal principle so venerable that it predates the common law itself: *volenti*

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[17] The concerns underlying the doctrines of standing, mootness, and ripeness often coincide. *See, e.g.*, 13 Charles Alan Wright et al., *Federal Practice and Procedure* § 3531, at 350 (2d ed. 1984) ("Both ripeness and mootness, indeed, could be seen as providing time-bound perspectives on the injury inquiry of standing."); *Warth*, 422 U.S. at 499 n.10 ("The standing question thus bears close affinity to questions of ripeness—whether the harm asserted has matured sufficiently to warrant judicial intervention—and of mootness—whether the occasion for judicial intervention persists.").

*non fit injuria*, or "to a willing person it is not wrong." *Black's Law Dictionary* 1605 (8th ed. 2004). That formulation comes from the *Liber Sextus* of Pope Boniface VIII in the late thirteenth century, but as a legal principle it actually dates back at least to the Codex of Justinian in 529 AD, and philosophically back to Aristotle. *See* Terence Ingman, *A History of the Defence of* Volenti Non Fit Injuria, 26 Jurid. Rev. 1, 1–3 (1981); N.G.L. Child, *"Volenti Non Fit Injuria,"* 17 Jurid. Rev. 43 (1905); Aristotle, Nichomachean Ethics, V. ix. 1136b ("no one can suffer injustice voluntarily, because no one can wish to be harmed"). In the absence of coercion or a public policy precluding consent, a voluntary payment is not an injury to legal rights, and is no business of the courts. *See, e.g.*, Restatement (Third) of Restitution and Unjust Enrichment § 6 cmt. d (T.D. No. 1, 2001) ("A transfer pursuant to a valid agreement of the parties cannot be nonconsensual, nor can it result in the unjustified enrichment of the recipient.").

MedImmune's voluntary payment of royalties therefore bears no resemblance to the payments that were made in *Altvater* and does not constitute injury sufficient to support jurisdiction. In *Altvater*, this Court rested its jurisdictional analysis on the same coercion principles, discussed above, that explain why a federal court has jurisdiction to evaluate pre-enforcement challenges to statutes and regulations. The patent owner had argued that, so long as the petitioner continued to pay royalties, there was not a justiciable controversy concerning the validity of the patent. 319 U.S. at 364.[18] This Court concluded that there was an actual controversy over the counterclaim because the royalties were being paid "under the compulsion of an injunction decree" from prior litigation between the parties, and "the

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[18] MedImmune wrongly suggests that the declaratory plaintiffs in *Altvater* were "licensees in good standing" not different from MedImmune. Pet. Br. 16. But in *Altvater* "both the District Court and the Circuit Court of Appeals have found that the license agreement was terminated on the surrender of the original patent and was not renewed and extended to cover the reissue patents." 319 U.S. at 364.

only other course" available was to "defy [an injunction]." *Id.* at 364–65. It reasoned that "the requirements of case or controversy are met where payment of a claim is demanded as of right and where payment is made, *but where the involuntary or coercive nature of the exaction preserves the right to recover the sums paid or to challenge the legality of the claim.*" *Id.* at 365 (emphasis added). This Court cited a treatise on quasi-contract and a string of its own cases, all making clear that a demand by a public official acting under color of law (*colore officii*) is inherently coercive, and that payments made under official pressure do not terminate the controversy over whether that demand was wrongful.[19]

MedImmune's payments are, by contrast, not an injury inflicted upon it, but simply the price of an insurance policy voluntarily purchased in 1997—and voluntarily renewed with each quarterly royalty payment—because MedImmune continues to regard that policy as worth the price. MedImmune has not repudiated that policy, does not genuinely contest its terms, and in fact took seven additional licenses after the Cabilly II Patent issued in order to insulate additional products in development from any risk under the patent laws. It has not been injured; it has gotten exactly what it paid for. MedImmune's curiosity about whether to abandon its license is not a controversy about legal rights; it is a request for judicial advice about the wisdom of a proposed business decision.

MedImmune has not repudiated the license or exercised its absolute right to terminate that agreement because doing so would expose it to the risk of the infringement suit. Managing that risk is the point of a license. If MedImmune

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[19] MedImmune misreads *Cardinal* and its discussion of *Altvater*. The only issue in *Cardinal* was whether a declaration of invalidity obtained by counterclaim when a "controversy" was plainly present should be vacated on appeal simply because the licensee also prevailed on the alternative ground of non-infringement. This Court simply held that it would not require the licensee to prove that it intended to "continue to violate the patentee's alleged rights" by making new, potentially infringing, products in order to retain the judgment it had already won. 508 U.S. at 100 n.22.

lost that suit it would (at a minimum) have to pay "reasonable royalty" damages that would be substantially higher than the highly favorable license rate it negotiated back in 1997 when Synagis had not been approved and Genentech had not been awarded the patent. (MedImmune itself agreed to a top royalty rate almost twice as high in the seven additional licenses to this patent that it negotiated in 2003. *Supra* at 6.) Nevertheless, MedImmune cannot retain all the benefits of its 1997 compromise while at the same time alleging that the payments it agreed to make constitute harm. That is contrary not only to *volenti non fit injuria* but also to the basic equitable principle that a party cannot take benefits under a contract and still challenge it as voidable. *Infra* at 42–44. If ever there were a claimed "injury" that is not cognizable in a court of law, this is it.[20]

For similar reasons, any injury MedImmune claims to be suffering from its payments is not "fairly traceable" to Genentech, but is instead self-inflicted and "traceable" only to MedImmune's own desire to avoid any risk under the patent laws. *Lujan*, 504 U.S. at 560; *see also McConnell*, 540 U.S. at 228 (candidates' claim of "competitive injury" was not fairly traceable to challenged statute because their "alleged inability to compete stems not from the operation of § 307, but from their own personal 'wish' not to solicit or accept large contributions, *i.e.*, their personal choice.").

**2. MedImmune Has Not Been Coerced**

The only way that MedImmune could characterize its royalty payments as an invasion of a legally protected interest would be to prove that those payments are coerced or involuntary. That is also precisely the showing it would have to make in order to establish the necessity that would

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[20] *Compare, e.g., McConnell*, 540 U.S. at 227 (an interest in competing in an election with equal resources is not cognizable injury); *Allen v. Wright*, 468 U.S. 737, 755–56 (1984) ("stigmatic injury" of racial discrimination "not judicially cognizable"); *United States v. Hays*, 515 U.S. 737, 746 (1995) (injury associated with living in segregated district not cognizable); *Lewis v. Casey*, 518 U.S. 343, 350–53 (1996) (rejecting prisoners' suit because injuries alleged did not pertain to any legal right).

justify an anticipatory "mirror image" declaration about the merits of the lawsuit that might result if it gave up its license. So MedImmune and the United States both implicitly acknowledge the correct analysis by arguing that MedImmune's royalty payments are "under protest" or are "coerced" by the consequences it could face if it gave up its license. Pet. Br. 24–25. Neither identifies anything special about this particular license; MedImmune and the United States assert that *all* patent licenses are legally coerced by "the inherently coercive backdrop of the presumption of validity and the powerful remedies afforded by the law to the patentee." U.S. Br. 21 & n.10; *see also* Pet. Br. 24–25.

That assertion cannot withstand serious scrutiny. The concept of legal coercion has been liberalized over time, but the one immutable certainty in this area of the law is that a payment made to resolve uncertain legal rights is never "coerced" by that uncertainty. As the 2005 draft of the Restatement (Third) of Unjust Enrichment explains (at § 6 cmt. d), any allegation of duress or mistake "disappears if the payment in question was made pursuant to a valid agreement of the parties allocating between them the risk of a perceived uncertainty as to the underlying obligation." This Court observed in *United States v. Child & Co.*, 79 U.S. 232, 245 (1871), that "[i]t is of the very essence of such adjustments of disputed rights that the contest shall be closed." If a party were permitted to challenge its own voluntary resolution of a potential legal dispute on the ground that it was "coerced" by the uncertain outcome of that suit, then "no party [could] safely pay [or accept] by way of compromise any sum less than what is claimed ..., for the compromise [would] be void as obtained by duress." *Id.* at 244. The same treatise and cases that this Court relied upon in *Altvater* make it perfectly clear that the potential consequences associated with losing an infringement suit could not possibly "coerce" MedImmune into purchasing immunity from suit by taking a license, and that "[p]rotest will not make an otherwise voluntary payment involuntary." Woodward, *supra*, at 388; *id* at 362–63 ("[P]ayment of a

claim under such circumstances would be an idle ceremony if the only effect were to reverse the parties as plaintiff and defendant ...."). The common law coercion cases MedImmune cites, Pet. Br. 24, are just the cases cited in *Altvater*, and all involved demands under color of official authority that the law regards as inherently coercive.

Patent licenses are squarely within the traditional rule that a contract designed to resolve uncertain legal rights cannot be "coerced" by that very uncertainty. A patent gives its owner "the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States." 35 U.S.C. § 154(a)(1). The patent laws grant patent holders a cause of action for infringement, and potential infringers various countervailing rights and defenses. The fundamental purpose and effect of a patent license is to resolve and compromise uncertainty concerning the parties' preexisting statutory rights under those laws. A license is therefore "an agreement manifestly intended to adjust conflicting rights" under the law. *Eureka Co. v. Bailey Co.*, 78 U.S. (11 Wall.) 488, 491 (1871); *see also, e.g.*, Carl Shapiro, *Antitrust Limits to Patent Settlements*, 34 Rand J. Econ. 391, 392 (2003) ("Virtually every patent license can be viewed as a settlement of a patent dispute ...."); *Blonder-Tongue*, 402 U.S. at 338 ("[P]rospective defendants will often decide that paying royalties under a license or other settlement is preferable to the costly burden of challenging the patent."); *Aronson v. Quick Point Pencil Co.*, 440 U.S. 257, 265 (1979) ("[T]he amount of leverage arising from a patent application depends on how likely the parties consider it to be that a valid patent will issue."). The nature of that bargain precludes, as a matter of law, any claim that the license was "coerced" by the licensee's fear that the patent might be valid. MedImmune's complaint that the parties' *ex ante* bargaining position was somehow coercive or unfair is simply disagreement with the statutory rights that Congress has chosen to give to patent holders.

Put another way, a license is no different from any other informal settlement of uncertain legal rights. This Court has repeatedly recognized that settlements render already-filed cases moot, requiring dismissal for lack of jurisdiction.[21] That is true "even if the parties remain at odds over the particular issue they are litigating." *ITT Rayonier Inc. v. United States*, 651 F.2d 343, 345 (5th Cir. 1983). A settlement reached *prior* to injury similarly prevents the incipient dispute from ripening into a justiciable controversy in the first place. There is no principled reason to treat a contract resolving a dispute *after a lawsuit is filed* as a jurisdictional termination of the controversy, but a contract resolving the same dispute before it ever ripens as a constitutional nullity.[22] Nor is there any reason to treat agreements labeled "settlements" differently from "licenses" that accomplish the same thing. The United States' suggestion that the license is "evidence of (not an obstacle to) a concrete controversy," U.S. Br. 21, is exactly backwards. A license resolves disputes about the parties' rights under the patent laws; it does not create them.

### 3. *Lear v. Adkins* Did Not Give Licensees A New Right To Challenge Validity Before Repudiating the License Agreement

As the Federal Circuit recognized, MedImmune's true argument must be that "under *Lear* it has the absolute right to challenge the validity or enforceability of the patent" even without repudiating its license. Pet. App. 4a. This suit is justiciable, in other words, only if *Lear* either creates a substantive right of challenge unknown at common law and not found in any statute, or abrogates basic *volenti non fit injuria* principles as inconsistent with patent policy.

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[21] *See Lake Coal Co. v. Roberts & Schaefer Co.*, 474 U.S. 120 (1985); *Bonner Mall*, 513 U.S. at 20; *see also, e.g.*, Charles Alan Wright, *Law of Federal Courts* § 12, at 62–63 (5th ed. 1994) ("There is no case or controversy once [a] matter has been resolved.").

[22] Unlike a pre-litigation resolution of legal uncertainty, a settlement procured after litigation has ensued may have *res judicata* effect. But that is no reason to treat them differently for justiciability purposes.

Neither theory is plausible. The common law held that the central purpose of a license is to terminate any dispute or uncertainty between the parties about their respective rights under the patent laws—including, most importantly, the validity of the patent—unless and until the licensee repudiated its benefits. Nothing in *Lear* is inconsistent with that understanding. *Lear* involved a licensee who had repudiated the benefits of the license and been sued by the licensor. *See* ABA Br. 3–4. It said nothing about a licensee, like MedImmune, who insists on keeping all the benefits of the license while challenging its basic premise.

The licensee estoppel doctrine discussed in *Lear* began at least three centuries ago as a principle of landlord-tenant law.[23] So long as a lessee retained quiet enjoyment of his property, common law courts held that he was estopped from challenging the title of his landlord. The principle goes back to Roman law, which held that a person could not refuse to return borrowed property on the ground that his lender had stolen it from someone else. *See Wilder v. Adams*, 29 F. Cas. 1216, 1218 (D. Mass 1846) (citing *inter alia* Dom. Civil Law. Pt 13, tit. 6; *Story on Bailments*, §§ 120, 230, 266). English and American courts soon extended this rule to hold that a licensee could not contest the validity of a licensed patent. The early cases rested in part on the equitable principle that a licensee cannot take the benefits of the license while challenging its fundamental premises, and also in part on a recognition that the patent's validity is simply irrelevant to the terms of the typical license bargain. Rooklidge, 8D-4 to -7, -12 n.57 & n.58. So long as the licensee retained "quiet enjoyment" of the benefits of the license (i.e., use of a presumptively valid patent free from fear of an infringement suit), the licensee

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[23] An appendix to the leading treatise on intellectual property licensing consolidates and reprints three articles that provide a scholarly overview of the early case law and its development. *See* William C. Rooklidge, *Licensee Validity Challenges and the Obligation to Pay Accrued Royaltics: Lear v. Adkins Revisited, reprinted in* 2 Roger M. Milgrim, *Milgrim on Licensing* Appendix 8-D (1994) (hereafter "Rooklidge").

got what it paid for. *See, e.g.*, *Bartlett v. Holbrook*, 67 Mass. 114, 118 (1854); *Marston v. Swett*, 66 N.Y. 206, 212 (1876).

The common law always recognized, however, that the estoppel ended if the licensee was "evicted" from quiet enjoyment (by a third-party decision declaring the patent invalid, or by widespread infringement) or if the licensee "evicted" itself by repudiating the benefits of the license. Rooklidge at 8D-10 to -11. Courts throughout the United States and England consistently applied the common law rule, including its exception for repudiating licensees, for more than a century and a half. *See, e.g.*, *Willison v. Watkins*, 28 U.S. 43, 48 (1830); *Kinsman v. Parkhurst*, 59 U.S. 289, 293 (1856); *Eureka Co.*, 78 U.S. (11 Wall.) at 491–92; ABA Br. 5–6.[24] Some doctrinal confusion crept in after this Court recognized in *St. Paul Plow Works v. Starling*, 140 U.S. 184 (1891), that a licensee's repudiation did not necessarily *terminate* the license as a contractual matter. The trial court in *St. Paul* correctly held that because of his repudiation the licensee was nonetheless permitted to raise invalidity as a defense, and this Court approved that holding *sub silentio*. But after *St. Paul* some courts lost sight of the equitable foundations of licensee estoppel and began to hold that the estoppel continued until the license terminated according to its terms—even if the licensee had clearly repudiated the benefits of the license. Rooklidge, 8D-16 & n.80 (collecting cases). And in *Automatic Radio Mfg. Co. v. Hazeltine*, 339 U.S. 827, 836 (1950), this Court stated that the "general rule is that the licensee under a patent license agreement may not challenge the validity of the licensed patent" without acknowledging a possibility of repudiation.

This pervasive confusion led to the California Supreme Court's holding in *Adkins v. Lear, Inc.*, 67 Cal. 2d 882 (1967),

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[24] MedImmune wrongly suggests that *Pope Manufacturing Co. v. Gormully*, 144 U.S. 224 (1892), rejected the common law rule. Pet. Br. 34. *Pope* held that a provision barring the licensee from challenging validity *after the license ended* violated public policy. *Pope* was fully consistent with the common law rule, as illustrated by this Court's continued application of estoppel to licensees who had not repudiated the license.

that a licensee is estopped from challenging validity despite clear repudiation of the license. This Court reacted very strongly against that holding in *Lear*, but it was only rejecting a deviation from the common law mainstream. Lear had clearly repudiated the agreement, was no longer accepting any benefits under the license, and had been sued for unpaid royalties. In that circumstance this Court concluded that "the equities of the licensor do not weigh very heavily." 395 U.S. at 670. The traditional common law agreed entirely.

Once it is understood that *Lear* was consistent with traditional limitations on the scope of licensee estoppel, the case for extending *Lear* to permit validity challenges by licensees, such as MedImmune, *that have not repudiated and wish to maintain all the benefits of the license* vanishes completely. That situation was not presented in *Lear*, and indeed Lear itself "conceded that it would be estopped to contest the validity of any patent issued to Adkins ... so long as it continued to operate under that agreement." *Id.* at 679 n.1 (White, J., concurring). This Court's statement that it was overruling the "*Hazeltine* rule" is as ambiguous as the *Hazeltine* opinion itself, and need not be read as rejecting centuries of common law jurisprudence that were not presented in *Lear* and that even Lear conceded. As this Court has explained, *Lear* "permits an accused infringer to accept a license, pay royalties for a time, and cease paying when financially able to litigate validity, secure in the knowledge that invalidity may be urged when the patentee-licensor sues for unpaid royalties." *Blonder-Tongue*, 402 U.S. at 346. There is no reason to read *Lear* more expansively when the lower courts have not done so,[25] and

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[25] Although one court initially concluded that *Lear* allowed a licensee to challenge the patent while still retaining its license, *see Warner-Jenkinson Co. v. Allied Chem. Corp.*, 567 F.2d 184 (2d Cir. 1977), most courts soon reaffirmed the common law distinction between licensees who repudiated and those who attempted to maintain the license. *See* ABA Br. 13. In *C.R. Bard, Inc. v. Schwartz*, 716 F.2d 874, 880–81 (Fed. Cir. 1983), decided well before the current crop of patents were issued, the

when that decision's broader rhetoric rests on premises that this Court has largely rejected. *See generally* Br. of Richard L. Donaldson *et al.* And certainly there is no justification for reading *Lear* to create a new substantive right to challenge patents, or to be free from voluntary royalty payments associated with invalid patents, when nothing in the patent laws suggests that Congress intended to create such a right and it would be inconsistent with basic common law principles. *See Mowry v. Whitney*, 81 U.S. 434, 441 (1872) (noting that the patent laws do not create a freestanding right for private persons to challenge patents); *Astoria Fed. Sav. & Loan Ass'n v. Solimino*, 501 U.S. 104, 108 (1991) ("Congress is understood to legislate against a background of common-law adjudicatory principles.").

MedImmune wrongly suggests that the Federal Circuit's decision somehow constitutionalizes the licensee estoppel doctrine, or makes it impossible for Congress to grant licensees a right to challenge patents. But Congress can always create new substantive rights in patent law, the invasion of which would confer standing and form the basis of a justiciable controversy. Congress could, for example, provide that patent licenses contain an implied warranty that the patent underlying the agreement is valid. (In this License Genentech expressly disclaimed any warranties.)

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Federal Circuit held that an Article III controversy existed in a validity challenge only because the licensee had "ceased payment of royalties," which was a "material breach of the agreement that ... enabled [the licensor] to terminate the agreement." And in 1997, before this license was signed, the Federal Circuit held that "a licensee ... cannot invoke the protection of the *Lear* doctrine until it (i) actually ceases payment of royalties, and (ii) provides notice to the licensor that the reason for ceasing payment of royalties is because it has deemed the relevant claims to be invalid." *Studiengesellschaft*, 112 F.3d at 1568. MedImmune's suggestion that the Federal Circuit's pre-*Gen-Probe* cases permitted suits like this is plainly incorrect. MedImmune's citation to 12 James W. Moore et el., *Moore's Federal Practice* § 57.22[8][c][i] (3d ed. 2005), Pet. Br. 19, adds nothing because *Moore's* merely cites *Warner-Jenkinson* and *C.R. Bard* and fails even to acknowledge that the Federal Circuit has long recognized that a non-repudiating licensee cannot sue for invalidity.

But MedImmune offers no serious argument that Congress has given it any legal right that is invaded either by its own royalty payments or by the bare existence of the patent.

### C. This Case Has Little In Common With Breach Of Contract Or Typical Patent Declaratory Cases

MedImmune labors to connect itself to cases granting declarations interpreting ambiguous contracts prior to breach. Its amici criticize the Federal Circuit's treatment of cases in which non-licensees seek a declaration about the scope or validity of a patent prior to infringement. None of these issues are relevant to the dispute in this case.

#### 1. This Is Not A Contract Dispute

MedImmune builds its argument around the idea that "patent-license controversies are a subset" of "[c]ontract disputes," Pet. Br. 30, and that the Declaratory Judgment Act was designed to permit interpretation of contracts prior to breach. The cases MedImmune discusses (Pet. Br. 20) are "mirror image" suits anticipating potential breach of contract actions, and seeking clarification of uncertainty about the parties' present legal rights and obligations under the contract. The lower courts have entertained such cases, although they are rarer than MedImmune implies and the courts often struggle with concerns about justiciability. Most of the decided cases have involved an imminent or "certainly impending" breach, and are therefore easy to justify on traditional principles. Contrary to MedImmune's implication, the analysis is never that because it is a contract case and no breach is required, anything goes.

Absent an imminent or reasonably certain breach, judicial intervention in contract disputes would have to be justified by the necessity or coercion principles at work in the pre-enforcement review cases or in the common law *quia timet* writ. That may or may not justify every decision on the books; the common law did not recognize the threat of private contract damages as legal coercion or as creating any necessity for early judicial intervention. In an appropriate case this Court might find a permissible extension of traditional principles, or it might not.

But this case is another kettle of fish. MedImmune does not even claim to fear contract damages, and there is no real dispute about its contract rights and obligations. Genentech expressly disclaimed any warranty that the patent is valid and MedImmune promised to pay royalties nonetheless. *Supra* at 6–7. MedImmune is not seeking an interpretation of its present contractual obligations at all; it wants a declaration of what its legal obligations *would be* if it chose to abandon its contract and opt into an entirely different legal regime. That has nothing to do with cases interpreting rights under a contract prior to breach.

At certain points MedImmune implies that there might be a contractual dispute over whether Synagis infringes the claims of the patent irrespective of validity, *i.e.*, whether Synagis is covered by the royalty-triggering language of the license. There is no genuine dispute on that issue, and if there ever was MedImmune has waived it. *Supra* at 9–11. Regardless, even if there were a genuine contractual dispute about non-infringement, that would not create a controversy over the issues of validity and enforceability.[26]

Any such claim also would not be sufficiently concrete or immediate to justify declaratory relief, because MedImmune never brought such concerns to Genentech to make sure it would disagree. Something like the "reasonable apprehension of suit" test is required by this Court's repeated holdings that there is no "necessity" for anticipatory adjudication of defenses to lawsuits or government enforcement actions that are unlikely to materialize.[27] All "mirror image" declaratory actions

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[26] *See Friends of the Earth, Inc. v. Laidlaw Envtl. Servs. (TOC), Inc.*, 528 U.S. 167, 185 (2000) ("[A] plaintiff must demonstrate standing separately for each form of relief sought."); *Lewis v. Casey*, 518 U.S. 343, 358 n.6 (1996) ("[S]tanding is not dispensed in gross.").

[27] *See, e.g., Poe v. Ullman*, 367 U.S. 497, 506 (1961) (stating that declaratory judgment procedure "does not permit litigants to invoke the power of this Court to obtain constitutional rulings in advance of necessity"). Understanding the precise nature of the suit the plaintiff fears is also essential to determining if federal question jurisdiction

therefore require a "reasonable apprehension of suit," although in many non-patent contexts it is fairly presumed. The basic insight behind the particular focus on "reasonable apprehension" in patent cases is that when a new product is marketed it may arguably infringe thousands of patent claims, although the vast majority of those claims will never be asserted. Hence, even the chief academic proponent of the Declaratory Judgment Act recognized that in patent cases some sharpening of the dispute between the parties is necessary to ensure that there is a real need for declaratory relief. *See, e.g.*, Edwin Borchard, *Declaratory Judgments* 807 (2d ed. 1941). When Genentech asserted that Synagis infringed its Cabilly I patent, MedImmune disagreed and produced evidence that convinced Genentech not to sue. *Supra* at 8. When Genentech asked MedImmune to clarify whether it believed Synagis infringed the Cabilly II patent, and if not then why, MedImmune declined to respond or to provide any explanation for its purported "protest." There is no necessity for "mirror image" declaratory relief when the plaintiff has not even procured a clear answer from the defendant. *Willing*, 277 U.S. at 288.

**2. Patent Declaratory Actions Brought By Non-Licensees Raise Different Concerns**

MedImmune and its amici also devote considerable ink to discussing cases in which a declaratory judgment plaintiff without a license seeks a "mirror image" declaration that a product it plans to sell does not infringe a patent, or that the patent in question is invalid. For over 40 years the lower courts have held that such cases are justiciable only if the declaratory plaintiff has put itself in a position to infringe the patent imminently, and has a "reasonable apprehension" that it will then be sued for infringement. Declaratory relief in the absence of imminent or "certainly impending" injury would, again, have to be justified by reference to coercion, necessity, and traditional equitable principles, and in an

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exists. Suits to enforce a license usually arise under state law. *See, e.g.*, *Skelly Oil Co. v. Phillips Petroleum Co.*, 339 U.S. 667, 672 (1950).

appropriate case this Court could strike that balance. *See, e.g., Woodworth v. Stone*, 30 F. Cas. 593, 594 (C.C.D. Mass. 1845) (Story, Circuit Justice) (noting that *quia timet* was available "upon well grounded proof of an apprehended intention of the defendant to violate the patent right"). But there certainly is no justification for an exception from ordinary justiciability rules when the prospective infringer has negotiated immunity from the suit it claims to fear.

MedImmune and its amici criticize the Federal Circuit's application of the reasonable apprehension test in patent cases brought by non-licensees, arguing for example that suits seeking a declaration of invalidity should not be dismissed simply because the patent holder has remained silent in the face of inquiries, or has chosen its words carefully to avoid any overt threat of an infringement suit. That is an interesting jurisprudential problem, but it is not remotely presented in this case. The party being coy about its intentions here was MedImmune, not Genentech. The basic issue in this case is not factual uncertainty over whether an infringement suit will materialize, but whether MedImmune should be allowed to seek a defensive declaration against an infringement suit that by definition *cannot* materialize unless MedImmune repudiates the license. In a case actually presenting the different problem identified by MedImmune's amici, this Court could adopt a rule that a "reasonable apprehension" exists whenever a prospective infringer directly asks the patent holder whether it intends to claim infringement, and gives the patent holder the information necessary to assess that question, and does not get a clear negative answer. *See Clair v. Kastar, Inc.*, 148 F.2d 644, 646 (2d Cir.) (L. Hand, J.) ("[I]f a manufacturer fears that he will be charged to infringe, he can always inquire of the patentee, and if the answer is unsatisfactory, he can bring an action for a declaratory judgment."), *cert. denied*, 326 U.S. 762 (1945). But a party cannot fear, or be legally coerced by, the threat of a lawsuit from which it has purchased immunity.

## II. THIS COURT SHOULD EXERCISE EQUITABLE DISCRETION TO DISMISS THIS SUIT

### A. The Declaratory Judgment Act Provides Broad Discretion To Decline Jurisdiction Based On Equitable Considerations

Even if this Court concludes that this case satisfies the minimum requirements for a constitutional controversy, or alternatively if it chooses to avoid that issue, it can and should direct dismissal on discretionary or prudential grounds. *See Steel Co.*, 523 U.S. at 97 & n.2; *Elk Grove Unified Sch. Dist. v. Newdow*, 542 U.S. 1, 11 (2004). In *Cardinal Chemical*, 508 U.S. at 99–102, this Court rejected the Federal Circuit's Article III reasoning but then addressed possible equitable arguments for reaching the same result that were not raised by either side. Because the Federal Circuit's Article III reasoning in *Gen-Probe* so clearly required dismissal, there was no cause or justification for Respondents to urge alternative arguments for the same result.[28] Regardless, the equitable and patent policy issues have been fully briefed at all stages of this case, and the Federal Circuit's jurisdictional reasoning (here as in *Gen-Probe*) was shaped in large part by those arguments.

Jurisdiction in declaratory judgment cases is always discretionary.[29] This Court has repeatedly held that courts should consider a broad range of equitable factors in striking "a proper balance between the needs of the plaintiff and the

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[28] *See Grosso v. United States*, 390 U.S. 62, 70–71 (1968) (failure to raise claim excused because of its futility in light of prevailing law). Genentech is entitled to raise alternative arguments for dismissing this case for lack of jurisdiction, under the "traditional rule" permitting parties to raise a "new argument in support of what has been [its] consistent claim" throughout the litigation. *Lebron v. Nat'l R.R. Passenger Corp.*, 513 U.S. 374, 379 (1995); *see also Yee v. City of Escondido*, 503 U.S. 519, 535 (1992).

[29] 28 U.S.C. § 2201(a) (court "may" grant declaratory relief); *Pub. Serv. Comm'n v. Wycoff*, 344 U.S. 237, 241 (1952) ("an enabling Act, which confers a discretion on the courts rather than an absolute right upon the litigant"); *Pub. Affairs Assocs., Inc. v. Rickover*, 369 U.S. 111, 112 (1962) (same); 10B Charles Alan Wright et al., *Federal Practice and Procedure* § 2759 (3d ed. 1998) (same).

consequences of giving the desired relief," *Eccles v. Peoples Bank of Lakewood Vill.*, 333 U.S. 426, 431 (1948), including traditional equitable defenses but also the broader public interest implicated by the suit.[30] As this Court observed in *Wilton v. Seven Falls Co.*, 515 U.S. 277, 287 (1995), if a court "know[s] at the commencement of litigation that it will exercise its broad statutory discretion to decline declaratory relief" on equitable grounds, it need not "go through the futile exercise of hearing [the] case on the merits first" and should simply decline jurisdiction at the outset. *See also Samuels v. Mackell*, 401 U.S. 66, 70 (1971).

Although this Court has indicated that discretion should ordinarily be exercised by district courts in the first instance, a remand in this case is unnecessary. The traditional equitable principles governing situations like this one are clear and categorical; this is a textbook case for the maxim that in appropriate circumstances equitable discretion may be "'hardened by experience into rule.'" *Wilton*, 515 U.S. at 289 (quoting Borchard, *Declaratory Judgments* 293); *see also Martin v. Franklin Capital Corp.*, 126 S. Ct. 704, 710 (2005) ("Discretion is not whim, and limiting discretion according to legal standards helps promote the basic principle of justice that like cases should be decided alike."). The Federal Circuit has already made clear that it believes suits like this one are inequitable. A

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[30] *See Abbott Labs*, 387 U.S. at 155 (because the Act provides equitable relief, "other equitable defenses may be interposed"); *Green v. Mansour*, 474 U.S. 64, 72 (1985) ("propriety of issuing a declaratory judgment may depend on equitable considerations"); *Great Lakes*, 319 U.S. at 300 ("The Declaratory Judgment Act was not devised to deprive courts of their equity powers or of their freedom to withhold relief upon established equitable principles."); *Ala. State Fed'n of Labor v. McAdory*, 325 U.S. 450, 462, 471 (1945) (relief must advance "the interests of justice" and serve the "public interest"); *Amoco Prod. Co. v. Vill. of Gambell*, 480 U.S. 531, 545 (1987) (observing "the important role of the "public interest" in the exercise of equitable discretion"). This Court has similarly advised against exercising jurisdiction over unripe claims, like MedImmune's, that are used to harass or to gain a procedural advantage. *See Wycoff*, 344 U.S. at 243; *Calderon v. Ashmus*, 523 U.S. 740, 747–48 (1998).

remand would serve no purpose but confusion. *See Pope*, 144 U.S. at 236–38 (dismissing patent license action on federal equitable principles); *City of Sherrill v. Oneida Indian Nation*, 544 U.S. 197 (2005) (applying equitable principles in the first instance to limit relief available); *Agostini v. Felton*, 521 U.S. 203 (1997) (applying equitable principles in the first instance to dissolve an injunction).

**B. This Suit Violates Basic Equitable Principles**

"As this Court has long recognized, 'a major departure from the long tradition of equity practice should not be lightly implied.'" *Ebay Inc. v. MercExchange, LLC*, 126 S. Ct. 1837, 1839 (2006) (citation omitted). MedImmune's suit violates settled canons of equity and at least three centuries of equitable tradition directly on point.

*First*, MedImmune's duplicitous "license and then sue" strategy violates the basic equitable principle that a party cannot accept benefits under an agreement while simultaneously attacking it as voidable. If a party to a contract learns that the contract was procured by fraud, for example, it must immediately choose between continuing to perform and to accept performance, or renouncing the contract and suing for fraud and rescission.[31] There is no

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[31] *See, e.g.*, Restatement (Second) of Contracts § 380 cmt. a (1981) ("A party who has the power of avoidance may lose it by action that manifests a willingness to go on with the contract. Such action is known as 'affirmance' and has the effect of ratifying the contract."); 27 Richard M. Lord, *Williston on Contracts* § 69:59 (4th ed. 2003) ("The defrauded party may lose his or her right of rescission by any act done after discovery of the fraud that indicates a willingness to allow the transaction to stand, such as the acceptance or demand of any benefit under the transaction."); Restatement (First) of Restitution § 68 cmt. b (1937) ("[A] person who receives or retains things to which he is entitled only if the transaction is binding thereby affirms it, if he knows the facts ...."); *Commodity Credit Corp. v. Rosenberg Bros. & Co.*, 243 F.2d 504, 512 (9th Cir.) ("[I]f, after full knowledge of the fraud or deceit, he goes forward and executes it notwithstanding such fraud, the damage which he thereby sustains is voluntarily incurred."), *cert. denied*, 355 U.S. 837 (1957); *Kingman & Co. v. Stoddard*, 85 F. 740, 745 (7th Cir. 1898) ("With respect to an executory contract, one may not, after knowledge of the fraud, continue to carry it out, exacting performance from the other party to it, receive its benefits,

reason to treat a licensee who contends that his license is unenforceable because the patent is invalid more generously than a licensee who contends that his license was procured by outright fraud. In either case the ancient and obviously correct principle is that the challenging party cannot have its cake and eat it too, but must choose whether it prefers the bargain or the *status quo ante*. If the licensee commits a material breach, the licensor always must elect between maintaining the license and suing for royalties, or terminating it and suing for infringement. *See, e.g., St. Paul*, 140 U.S. at 196; *United Mfg. & Serv. Co. v. Holwin Corp.*, 187 F.2d 902, 905 (7th Cir. 1951) ("[W]hile the license agreement is still in effect the owner of the patent cannot sue for infringement. He is limited to the enforcement of his rights and remedies under the license agreement.").

MedImmune wants to avoid that choice, keeping the favorable royalty rate it received from Genentech in exchange for early "patent peace" while destroying the premises of that bargain. Its own conduct makes clear that MedImmune understands the inherent duplicity of this strategy. After deciding to file this lawsuit, it kept silent about that decision and spent the better part of a year sewing up seven additional licenses to cover other products then in development. Only after obtaining those licenses did MedImmune file this suit less than three months later. J.A. 437; *supra* at 9–10. Its parallel conduct with Centocor vividly illustrates that MedImmune's conduct is part of a broader and deliberate strategy. *Supra* at 10 n.7. That behavior is not clever; it is fundamentally inequitable.[32] Its only real excuse—that it could not know the claims of the

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and still pursue an action for deceit ....").

[32] In a similar vein, courts have repeatedly dismissed patent declaratory judgment actions when it appears that the licensee signed a licensing agreement only to buy itself more time to forum shop and prepare litigation papers before breaching the license. *See, e.g., Mission Ins. Co. v. Puritan Fashions Corp.*, 706 F.2d 599, 602 n.3 (5th Cir. 1983); *Charles Schwab & Co. v. Duffy*, 49 U.S.P.Q.2d (BNA) 1862 (N.D. Cal. 1998).

patent at the time it agreed to the license—is both factually unsupportable, *supra* at 4–5, and legally irrelevant.[33]

*Second*, MedImmune's suit is obviously inconsistent with the even more specific, and directly on point, equitable tradition of licensee estoppel. As noted, *supra* at 32–33, common law judges thought long and hard about whether a licensee in good standing could bring a validity challenge consistent with equitable principles while continuing to enjoy the benefits of the license. For at least three centuries they answered with a consistent and emphatic "no." The common law was not blind to the public policies that favor (within limits) judicial challenges to patents that may be invalid, but sensibly balanced the relevant policies in the same way this Court did on the facts of *Lear* itself: by giving licensees an option to repudiate the license and defend any resulting suit on the ground that the patent was invalid. MedImmune's only refuge is to argue that under *Lear* all considerations of equity and tradition must be ignored deference to a particular conception of patent policy in which nothing matters but encouraging patent litigation. *Lear* does not remotely require that result.

### C. Adjudication Of Licensee Challenges To Validity Prior To Repudiation Frustrates The Core Purposes Of The Patent Laws

MedImmune's policy arguments collapse into a belief that licensors and licensees should be forced to internalize risks they are currently choosing to share and bear costs they are currently contracting to avoid, and that more of our country's productive resources should be devoted to patent litigation and less toward research and development of new

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[33] Restatement (Second) of Contracts § 154 (1981) (party to a contract always bears the risk of mistake if "he is aware, at the time the contract is made, that he has only limited knowledge with respect to the facts to which the mistake relates but treats his limited knowledge as sufficient"); William A. Keener, *A Treatise on the Law of Quasi-Contracts* § 42 (1926) ("[I]f one is conscious of a doubt as to his legal rights or duties, and with or without deliberation, with or without advice, chooses and enters upon a course of action, he should not be permitted to repudiate his choice.").

technologies. It urges this Court to be the agent of such a revolution on the premise that the system Congress established for reviewing patent applications is fundamentally broken, that most issued patents are invalid, and that therefore the public interest cannot tolerate licensees bargaining away (even temporarily and with regard to themselves alone) the ability to file lawsuits like this one. This agitation should be directed to Congress. *See, e.g., Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 168 (1989) ("It is for Congress to determine if the present system of design and utility patents is ineffectual in promoting the useful arts in the context of industrial design."). Congress has considered policy arguments like these for decades, and has repeatedly declined to codify any statutory extension of *Lear*, to create any general cause of action to challenge the validity of a patent, or even to modify the rule that all patents are to be presumed valid, 35 U.S.C. § 282.[34] What Congress has done instead is to create a cost-efficient, expeditious new *administrative* process for reexamination of patents before the PTO. 35 U.S.C. § 303(a).[35] MedImmune admits that it has not only invoked that procedure in this case, but that the reexamination process has allowed it to present the challenges to the Cabilly II patent that it attempts to raise in this declaratory judgment suit. *See* Pet. Br. 48 n.18. Against that backdrop, MedImmune's rhetoric about the need for this Court to save the country from a plague of invalid patents rings hollow.

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[34] *See* Resp. City of Hope Br. at 41. As one of MedImmune's amici notes, a bill is pending before the House of Representatives that would provide a system of post-grant review of issued patents, including the right of any dissatisfied party to appeal the determination to the Federal Circuit. *See* H.R. 2795, 109th Cong. § 9 (introduced June 8, 2005).

[35] Even the Federal Trade Commission, which regulates anticompetitive conduct, has not recommended what MedImmune proposes here. In 2003, it suggested changes to *the administrative process* for reexamination; it did not suggest Congress give licensees a cause of action to challenge a patent's validity. *See* FTC, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy*, ch. 5, at 23–24 (Oct. 2003), *available at* http://www.ftc.gov/os/2003/10/innovationrpt.pdf.

Regardless, MedImmune's policy analysis considers only the potential benefits that would be produced by taking some invalid patents off the books, but completely ignores the associated costs—in the form of greatly increased litigation expenses, decreased licensing, and decreased use of the patent system. It would encourage more challenges to patents by licensees, at the expense of decreasing the number of licensees and the number of productive collaborations facilitated by licensing, as well as overall use of the patent system and investments in research and innovation. *See* John W. Schlicher, *Judicial Regulation of Patent Licensing, Litigation and Settlement Under Judicial Policies Created in* Lear v. Adkins, *in* American Intellectual Property Law Association, *Selected Legal Papers*, Vol. III, No. 1, I-8 to -13 (June 1985). Those trade-offs are complex and not well suited to judicial resolution.

*First*, MedImmune's proposal would inflict enormous deadweight social costs. The effects on price and output are explained in detail in the literature,[36] but the basic principles are simple. Under the common law rule, a licensor's freedom from the risk and expense of patent litigation (limited, of course, by the licensee's right to repudiate) creates value for the licensor and decreases the price at which it will grant a license. MedImmune's proposed rule encourages licensees to sue whenever expected future royalties multiplied by the chance of establishing invalidity exceed the likely litigation costs. Where as here the royalties are many multiples of the litigation costs, a licensee would arguably breach its fiduciary duty to its shareholders by not taking a shot at suit. MedImmune's proposed rule would also have the perverse effect of encouraging patent holders to file infringement suits against prospective licensees and then explicitly "settle" the litigation via a license, to achieve res judicata protection from any subsequent validity challenge.

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[36] *E.g.*, John W. Schlicher, *A Lear v. Adkins Allegory*, 68 J. Pat. & Trademark Off. Soc'y 427, 429–35 (1986); Schlicher, *Judicial Regulation of Patent Licensing*, I–8 to –13.

As MedImmune concedes, the patent litigation its rule would instigate would be enormously expensive. Pet. Br. 44–45 (estimating legal costs of challenge at $5–$7 million). If licensees can no longer credibly promise to pay royalties in exchange for "patent peace," the licensor has no choice but to factor litigation costs into the profit maximizing royalty rate. That will necessarily discourage some licensees from taking a license, and decrease the output of the rest. *See* Schlicher, *Judicial Regulation of Patent Licensing* at I–8 to –11. Licenses are socially beneficial because they encourage production and innovation that might not otherwise occur, or that might otherwise remain with a less efficient firm (such as the patent holder itself). *Id.* at I–11 to –12 (increase in licensing costs will lead to "monopolistic exploitation at higher costs"); *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 487 (1974). The sharing of technology under patent licenses is also essential to the collaborative research environment that has made the past decades' dramatic advances in medicine and biotechnology possible. Individual firms, each exploiting only their own patented techniques, would never produce innovation at the current breakneck pace.

MedImmune misses the point by arguing that small start-up companies often agree to licenses only because they are initially "unable to afford the high cost of patent litigation." Pet. Br. 45. MedImmune's proposed rule would force patent holders to internalize projected litigation costs into the price of a license, and the entrepreneurs it purports to be concerned about would then be unable to afford a license. The United States concedes as much by acknowledging that patent holders would inevitably respond to MedImmune's rule by requiring paid-in-full up-front licenses, U.S. Br. 28–29, which will price many prospective licensees (and particularly cash-poor startup companies) out of the license market entirely. And in many industries, parties structure patent licenses to defer royalty payments until the point where the licensee actually markets a product or service subject to the license. The ability to

defer royalty payments therefore provides the licensee with more discretion over the decision to use the patented invention in its products. A license agreement that frontloads payments necessarily requires licensees to decide prior to entering the license whether they will proceed all the way with development in a manner that uses the patent.

*Second*, by greatly decreasing the value of licensing to both parties, MedImmune's rule also decreases the net expected value of a patent itself, with predictably negative consequences for use of the patent system and perhaps for overall investments in innovation. An inventor considering whether to invest in research and development faces enormous risks associated with whether that investment can ultimately be recouped. If a patent is applied for and granted, the patent system requires complete public disclosure of the invention. If that patent is later set aside as invalid, then the public gets a free ride on the inventor's efforts and investment. Traditional licenses make it possible to share that risk. But MedImmune's proposed rule forces the inventor to bear it all alone, and also imposes a large and unavoidable risk of expensive litigation on anyone brash enough to apply for a patent. The predictable result is to make the patent system less appealing, giving inventors an incentive to either decrease their innovative activities or maintain those efforts but opt-out of the patent system and rely on state trade secret law—which is a far inferior outcome from the standpoint of public policy.

MedImmune's real complaint in this litigation is that the bargaining leverage Genentech had before MedImmune took a license, and that Genentech would have again if MedImmune repudiated that license, is unfair and should be regarded as legal coercion. MedImmune fears that if it repudiated the license, sued for a declaration of invalidity, and lost, Genentech would not give it a new license at the same favorable royalty rate it now enjoys. But Congress gave patent holders "the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention

into the United States." 35 U.S.C. § 154(a)(1). There is no public policy demanding that MedImmune have a license from Genentech, or that it retain the favorable royalty rate it negotiated back in 1997. As this Court has often observed, compulsory licensing "is a rarity in our patent system." *Dawson Chem. Co. v. Rohm & Haas Co.*, 448 U.S. 176, 215 & n.21 (1980). Although "[c]ompulsory licensing of patents often has been proposed," it "has never been enacted on a broad scale."[37] So, like it or not, MedImmune must choose between litigating or licensing.

The United States concedes that MedImmune's proposal to increase patent litigation is bad policy, by suggesting that it will not work,[38] by conspicuously emphasizing that it will not apply to the United States' *own* patents in any event, U.S. Br. 23 n.11, and by suggesting various ways that inventors might be able to contract to avoid it, such as "requir[ing] prospective licensees to purchase a fully paid-up license" or including a provision making explicit that lawsuits like MedImmune's constitute a material breach of the license. U.S. Br. 28–29. The United States is, of course, correct that licensors would inevitably respond to a victory by MedImmune in this case by demanding large up-front payments rather than ongoing royalties, but that shift will just discourage licensing without even encouraging validity challenges. A licensee that has already paid in full has *no incentive to challenge validity*, ever.

More broadly, the United States' suggestion cuts the heart out of its (and MedImmune's) arguments on the merits. If public policy somehow demands that licensees be unfettered and have a strong incentive to challenge validity,

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[37] 448 U.S. at 215 n.21; *see Hartford-Empire Co. v. United States*, 323 U.S. 386, 417 (1945) (observing that "Congress was asked as early as 1877, and frequently since, to adopt a system of compulsory licensing of patents" but "[i]t has failed to enact these proposals into law"); *Dawson Chem.*, 448 U.S. at 215 n.21 ("compulsory licensing provisions were considered for possible incorporation into the 1952 revision of the patent laws").

[38] U.S. Br. 26 (arguing that litigation costs will deter challenges and "[m]any patents are clearly valid, and thus are unlikely to be challenged").

then why hypothesize or permit ways that the parties could evade that policy? The answer, of course, is that the United States recognizes that MedImmune's rule may be inefficient and undesirable, and does not want to limit the parties' contractual freedom. But if this case just boils down to determining what the right presumption or contractual default rule should be, then surely the right choice is the common law rule that Congress has never altered, which for centuries has recognized that suits like this one are fundamentally inconsistent with the bargain at the heart of a license, and which notwithstanding the confusion briefly introduced by *Lear* has been reaffirmed as sound precedent. The patent system does not need the United States' various suggestions, particularly since it simultaneously invites decades of litigation and confusion by speculating that its proposals might or might not be unenforceable for public policy reasons. *See* Licensing Exec. Society Br. 12.

There is no justiciable controversy in this case, but even if there were, it is not a case that any court of equity should reach out to hear. MedImmune is trying simultaneously to receive and challenge the benefit of its bargain, in direct conflict with centuries of equitable jurisprudence directly on point. In this area as in many others, "a page of history is worth a volume of logic." *N.Y. Trust Co. v. Eisner*, 256 U.S. 345, 349 (1921) (Holmes, J.). The traditional understanding that a license resolves any cognizable dispute over the validity of the patent, unless and until the licensee is willing to repudiate the benefits of its bargain, strikes a sensible balance both as a matter of equity and public policy. If that traditional presumption needs to change, the change should come from Congress.

## CONCLUSION

For the reasons set forth, this Court should affirm the judgment of the Court of Appeals.

Respectfully submitted,


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# ADDENDUM

## CONSTITUTIONAL AND STATUTORY PROVISIONS INVOLVED

**U.S. Const. Art. III, § 2, cl. 1**

The judicial Power shall extend to all Cases, in Law and Equity, arising under this Constitution, the Laws of the United States, and Treaties made, or which shall be made, under their Authority;—to all Cases affecting Ambassadors, other public Ministers and Consuls;—to all Cases of admiralty and maritime Jurisdiction;—to Controversies to which the United States shall be a Party;—to Controversies between two or more States;—between a State and Citizens of another State;—between Citizens of different States;—between Citizens of the same State claiming Lands under Grants of different States, and between a State, or the Citizens thereof, and foreign States, Citizens or Subjects.

**28 U.S.C. § 2201. Creation of remedy**

(a) In a case of actual controversy within its jurisdiction, except with respect to Federal taxes other than actions brought under section 7428 of the Internal Revenue Code of 1986, a proceeding under section 505 or 1146 of title 11, or in any civil action involving an antidumping or countervailing duty proceeding regarding a class or kind of merchandise of a free trade area country (as defined in section 516A(f)(10) of the Tariff Act of 1930), as determined by the administering authority, any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested party seeking such declaration, whether or not further relief is or could be sought. Any such declaration shall have the force and effect of a final judgment or decree and shall be reviewable as such.

(b) For limitations on actions brought with respect to drug patents see section 505 or 512 of the Federal Food, Drug, and Cosmetic Act.

**35 U.S.C. § 120. Benefit of earlier filing date in the United States**

An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application. No application shall be entitled to the benefit of an earlier filed application under this section unless an amendment containing the specific reference to the earlier filed application is submitted at such time during the pendency of the application as required by the Director. The Director may consider the failure to submit such an amendment within that time period as a waiver of any benefit under this section. The Director may establish procedures, including the payment of a surcharge, to accept an unintentionally delayed submission of an amendment under this section.

**35 U.S.C. § 132(a). Notice of rejection; reexamination**

Whenever, on examination, any claim for a patent is rejected, or any objection or requirement made, the Director shall notify the applicant thereof, stating the reasons for such rejection, or objection or requirement,

together with such information and references as may be useful in judging of the propriety of continuing the prosecution of his application; and if after receiving such notice, the applicant persists in his claim for a patent, with or without amendment, the application shall be reexamined. No amendment shall introduce new matter into the disclosure of the invention.

**35 U.S.C. § 135(a). Interferences**

Whenever an application is made for a patent which, in the opinion of the Director, would interfere with any pending application, or with any unexpired patent, an interference may be declared and the Director shall give notice of such declaration to the applicants, or applicant and patentee, as the case may be. The Board of Patent Appeals and Interferences shall determine questions of priority of the inventions and may determine questions of patentability. Any final decision, if adverse to the claim of an applicant, shall constitute the final refusal by the Patent and Trademark Office of the claims involved, and the Director may issue a patent to the applicant who is adjudged the prior inventor. A final judgment adverse to a patentee from which no appeal or other review has been or can be taken or had shall constitute cancellation of the claims involved in the patent, and notice of such cancellation shall be endorsed on copies of the patent distributed after such cancellation by the Patent and Trademark Office.

**35 U.S.C. § 146. Civil action in case of interference**

Any party to an interference dissatisfied with the decision of the Board of Patent Appeals and Interferences on the interference, may have remedy by civil action, if commenced within such time after such decision, not less than sixty days, as the Director appoints or as provided in section 141

of this title, unless he has appealed to the United States Court of Appeals for the Federal Circuit, and such appeal is pending or has been decided. In such suits the record in the Patent and Trademark Office shall be admitted on motion of either party upon the terms and conditions as to costs, expenses, and the further cross-examination of the witnesses as the court imposes, without prejudice to the right of the parties to take further testimony. The testimony and exhibits of the record in the Patent and Trademark Office when admitted shall have the same effect as if originally taken and produced in the suit.

Such suit may be instituted against the party in interest as shown by the records of the Patent and Trademark Office at the time of the decision complained of, but any party in interest may become a party to the action. If there be adverse parties residing in a plurality of districts not embraced within the same state, or an adverse party residing in a foreign country, the United States District Court for the District of Columbia shall have jurisdiction and may issue summons against the adverse parties directed to the marshal of any district in which any adverse party resides. Summons against adverse parties residing in foreign countries may be served by publication or otherwise as the court directs. The Director shall not be a necessary party but he shall be notified of the filing of the suit by the clerk of the court in which it is filed and shall have the right to intervene. Judgment of the court in favor of the right of an applicant to a patent shall authorize the Director to issue such patent on the filing in the Patent and Trademark Office of a certified copy of the judgment and on compliance with the requirements of law.

**35 U.S.C. § 154(a)(1). Contents and term of patent; provisional rights**

Every patent shall contain a short title of the invention and a grant to the patentee, his heirs or assigns, of the right to

exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States, and, if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States, or importing into the United States, products made by that process, referring to the specification for the particulars thereof.

**35 U.S.C. § 282. Presumption of validity; defenses**

A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. Notwithstanding the preceding sentence, if a claim to a composition of matter is held invalid and that claim was the basis of a determination of nonobviousness under section 103(b)(1), the process shall no longer be considered nonobvious solely on the basis of section 103(b)(1). The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.

The following shall be defenses in any action involving the validity or infringement of a patent and shall be pleaded:

(1) Noninfringement, absence of liability for infringement or unenforceability,

(2) Invalidity of the patent or any claim in suit on any ground specified in part II of this title as a condition for patentability,

(3) Invalidity of the patent or any claim in suit for failure to comply with any requirement of sections 112 or 251 of this title,

(4) Any other fact or act made a defense by this title.

In actions involving the validity or infringement of a patent the party asserting invalidity or noninfringement shall give notice in the pleadings or otherwise in writing to the adverse party at least thirty days before the trial, of the country, number, date, and name of the patentee of any patent, the title, date, and page numbers of any publication to be relied upon as anticipation of the patent in suit or, except in actions in the United States Court of Federal Claims, as showing the state of the art, and the name and address of any person who may be relied upon as the prior inventor or as having prior knowledge of or as having previously used or offered for sale the invention of the patent in suit. In the absence of such notice proof of the said matters may not be made at the trial except on such terms as the court requires. Invalidity of the extension of a patent term or any portion thereof under section 154(b) or 156 of this title because of the material failure—

(1) by the applicant for the extension, or

(2) by the Director,

to comply with the requirements of such section shall be a defense in any action involving the infringement of a patent during the period of the extension of its term and shall be pleaded. A due diligence determination under section 156(d)(2) is not subject to review in such an action.

35 U.S.C. § 303. Determination of issue by Director

(a) Within three months following the filing of a request for reexamination under the provisions of section 302 of this

title, the Director will determine whether a substantial new question of patentability affecting any claim of the patent concerned is raised by the request, with or without consideration of other patents or printed publications. On his own initiative, and any time, the Director may determine whether a substantial new question of patentability is raised by patents and publications discovered by him or cited under the provisions of section 301 of this title. The existence of a substantial new question of patentability is not precluded by the fact that a patent or printed publication was previously cited by or to the Office or considered by the Office.

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IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,
*Petitioner*,

v.

GENENTECH, INC., *et al.*,
*Respondents*.

**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## REPLY BRIEF FOR PETITIONER

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## REPLY BRIEF FOR PETITIONER

At issue is whether petitioner as a patent licensee is barred from the federal courts for continuing to pay royalties while disputing the validity, enforceability and infringement of the patent. The Federal Circuit insists that to resolve the dispute in federal court, a licensee first must raise the stakes by ceasing payment and inviting charges of breach of contract and patent infringement. That is hardly a practical solution to a recurrent kind of business disagreement; it is not demanded by Article III; and it is exactly the sort of wasteful behavior, costly to all parties, that the Declaratory Judgment Act was enacted to make unnecessary.

The Declaratory Judgment Act authorizes relief to "declare the rights and other legal relations" of "any interested party" in a "case of actual controversy" within the jurisdiction of the federal courts. 28 U.S.C. § 2201(a). Under decisions of this Court followed for seven decades, the provisions of that statute, and the Article III requirements it incorporates, are satisfied. The Federal Circuit decision under review, and the one two years ago that gave rise to it,[1] were a mistaken deviation.

What respondents seek "would amount to a significant revision of our precedent interpreting Article III." *Daimler-Chrysler Corp.* v. *Cuno*, 126 S. Ct. 1854, 1867 (2006). Nor would such a revision well serve the patent laws. "Licensees may often be the only individuals with enough economic incentive to challenge the patentability of an inventor's discovery. If they are muzzled, the public may continually be required to pay tribute to would-be monopolists without need or justification." *Lear, Inc.* v. *Adkins*, 395 U.S. 653, 670 (1969).

### 1. The Governing Decisions.

Federal declaratory-judgment law began with three significant decisions by this Court during the decade after the Act was passed. This case fits comfortably within those deci-

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[1] *Gen-Probe Inc.* v. *Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir.), *pet'n for cert. dismissed*, 543 U.S. 941 (2004).

sions, which have stood unchallenged and respected for three generations. Respondents' arguments strikingly resemble those made unsuccessfully in the 1930s and 1940s.[2]

1. Respondents seek to discount this Court's foundational decision in *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227 (1937), setting it aside as simply a "mirror image" "symmetrical" suit, Gen. 21; COH 15. Respondents ignore not only *Aetna's* principle but its facts. None of the five insurance policies in *Aetna* required payment to the beneficiary spouse until the death of the insured husband. 300 U.S. at 237. Three called for no other payments; two provided for small payments to the husband in the event of permanent disability, but it was argued without contradiction that those amounts were too small to satisfy the federal jurisdictional amount, see 300 U.S. at 234 (argument for respondents), an issue this Court found unnecessary to reach. 300 U.S. at 243. This Court sustained jurisdiction as to all policies and both defendants.

2. *Maryland Cas. Co.* v. *Pacific Coal & Oil Co.*, 312 U.S. 270 (1941), contains perhaps the most succinct (and often quoted) statement of what declaratory actions require: "a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality." *Id.* at 273. Each of those requirements is met here, and respondents never

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[2] *E.g.*, Gen. 1, 16, 27 ("judicial advice"), 14, 15, 16, 17 ("hypothetical"), 25 ("injury . . . will likely never occur"); COH 11 ("obtaining advice") ("contingency that may never occur"), 22, 29, 30 ("no ripe controversy"), 19, 20, 21 ("hypothetical"), 31 ("entirely contingent and remote") ("MedImmune has the unilateral power to decide"). *Compare* the opinion this Court reversed in *Aetna*: "advisory opinions;" "no suit is threatened and no demand made by the defendants;" "[t]he right of cancellation is one which the plaintiff may exercise itself without asking the aid of the court;" "too remote and vague;" "do not show that any right of the plaintiff is presently being invaded or imminently and prejudicially affected." *Aetna Life Ins. Co.* v. *Haworth*, 84 F.2d 695, 697-98 (8th Cir. 1936), *rev'd*, 300 U.S. 227 (1937). "Gen." and "COH" refer to respondents' respective briefs, "C.A.A." to the joint appendix in the Court of Appeals.

directly respond to them. Genentech scarcely mentions *Maryland Casualty*, grouping it as a "mirror image" case, but acknowledging that the collision victim defendant in that case had not sued the insurer (and, having brought an action against only the insured in state court, could not have done so without first winning a judgment). Gen. 21 & n.13; see also COH 16. The rule of *Maryland Casualty*, which has stood the test of decades, is the established rule. The present dispute certainly has no less "immediacy and reality" than the potential claim held sufficient in *Maryland Casualty*.

3. *Altvater* v. *Freeman*, 319 U.S. 359 (1943), is inescapable for its specific holding in the patent-license context that a party making royalty payments is not thereby placed outside the Declaratory Judgment Act:

> "It is said that so long as petitioners are paying royalties . . . there is only an academic, not a real controversy, between the parties. . . . *The fact that royalties were being paid did not make this a 'difference or dispute of a hypothetical or abstract character.'*"

319 U.S. at 364, quoting *Aetna*, 300 U.S. at 240 (emphasis supplied). Respondents would disregard *Altvater* because the license royalty payments there had been reinforced by an injunction. Gen. 26-27; COH 24-25.[3] But this Court emphasized that the royalty payments (there as here "under protest") were made not only in accordance with the injunction, but also because not to pay would "risk not only actual but treble damages in infringement suits." *Id.* at 365. *Altvater* recognized that risk of treble damages, as well as of other sanctions, independently satisfied Article III and the Declaratory Judgment Act.

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[3] Although the lower courts had ruled the license itself no longer applicable, the injunction implementing it remained in effect and, along with the risk of infringement penalties, "preserve[d] the right . . . to challenge the legality of the claim," as the licensees continued to pay royalties in the amounts required by the license. 319 U.S. at 362, 365.

**2. "Reasonable Apprehension of Suit."**

The Federal Circuit held that Article III requires more than a concrete and immediate dispute as to legal rights—the standard of *Maryland Casualty*—but also a "reasonable apprehension of suit"—which, it went on to hold, as a matter of law cannot exist if a licensee is in good standing paying royalties. P.C.A. 4a-6a.

Respondents strenuously argued for that rule in the Court of Appeals, Gen. C.A. Br. 21, COH C.A. Br. 7-8, and they defended it, as their lead argument, in their opposition to certiorari. Br. Opp. 8-10, 16 ("the point itself is unassailable"). City of Hope now disowns the rule, saying that it "confused matters" and "is not at issue here," because the Federal Circuit additionally requires that a declaratory plaintiff be "actually or imminently engaging in allegedly infringing conduct," and that "is not satisfied here." COH 29. But the record is undisputed that Genentech demanded royalties on the ground that Synagis® was an infringing product that petitioner was manufacturing and selling. J.A. 419, 428. City of Hope otherwise concedes that whether "reasonable apprehension of suit" is a part of Article III "might well raise questions that merit the Court's attention in some future case." COH 30. Genentech likewise offers little defense of "reasonable apprehension of suit." It vaguely suggests that the Federal Circuit's rule "captures the right concept," Gen. 14, discerns "[s]omething like" it in the cases, *id.* 37, but calls it "an interesting jurisprudential problem" not to be addressed here, *id.* 39.

Respondents apparently have come to recognize that "reasonable apprehension of suit"—defined by the Federal Circuit to exclude all licensees in good standing—is irreconcilable with *Maryland Casualty* and *Aetna*, as well as with this Court's explanation in *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83, 96 (1993), that "[m]erely the desire to avoid the threat of a 'scarecrow' patent" may satisfy the Declaratory Judgment Act. "The existence of an invalid

patent may substantially impair the economic position of those who market articles which infringe such a patent, even though no infringement suits may be immediately threatened." *Altvater*, 319 U.S. at 371 (opinion of Frankfurter, J.).

**3. Justiciability.**

Avoiding the decisive precedents, respondents have turned instead to what they call "basic legal principles going back 1500 years," Gen. 14, plus a list of textbook Article III objections. Respondents' project to reconstitute Article III declaratory-judgment law leads them to disdain decisions of the Second Circuit ("confusion"), the Third Circuit ("semantic imprecision"), the Seventh Circuit (same), COH 39 & n.20, and even of this Court ("*Lear* reflected *Hazeltine*'s confusion;" "extravagant patent misuse theories;" "one-sidedness was a defect in *Lear*"), *id.* 37, 41. Respondents also reject leading treatises. Gen. 35 n.25 (faulting *Moore's* for relying on the cases that rejected respondents' position). Respondents further complain of "other cases where lower courts have adjudicated declaratory claims in the absence of a ripe conventional controversy under Article III." COH 20. On the other hand, respondents repeatedly rely on decisions long overruled.[4]

**A. *Standing.***

1. Respondents challenge standing. The Declaratory Judgment Act allows relief for "any interested party." 28 U.S.C. § 2201(a). Petitioner is a very "interested party." Facing multi-million-dollar royalty payments on the one hand, and risk of injunction, treble damages and other sanctions on the other, petitioner is the most interested party imaginable, not "everyman." *Bennett* v. *Spear*, 520 U.S. 154, 166 (1997).

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[4] In addition to several pre-*Lear* cases, Genentech twice cites *Willing* v. *Chicago Auditorium Ass'n*, 277 U.S. 274 (1928), which cast doubt on whether Article III would permit federal courts to rule on declaratory judgments. Gen. 22 n.15, 38. Five years later in *Nashville, C. & St. L. Ry.* v. *Wallace*, 288 U.S. 249, 262 (1933), this Court unanimously held otherwise and left *Willing* "explained away" and "in effect . . . overruled." Borchard, *Justiciability*, 4 U. CHI. L. REV. 1, 3-4 (1936).

Petitioner "personally has suffered some actual or threatened injury" that "fairly can be traced to the challenged action" of respondents and will be "redressed by a favorable decision." *Valley Forge Christian College* v. *Americans United for Separation of Church & State, Inc.*, 454 U.S. 464, 472 (1982) (internal quotation marks omitted); *Lujan* v. *Defenders of Wildlife*, 504 U.S. 555, 560-61 (1992). And the dispute arises in "a concrete factual context." *Valley Forge*, 454 U.S. at 472. This is not a case about "value interests of concerned bystanders." *Id.* at 473, quoting *United States* v. *SCRAP*, 412 U.S. 669, 687 (1973); *cf. DaimlerChrysler*, 126 S. Ct. at 1864 (rejecting taxpayer standing). This is not a complaint asserting a vague intention to visit Sri Lanka some day. *Lujan*, 504 U.S. at 563-64.

*Vermont Agency* v. *United States ex rel. Stevens*, 529 U.S. 765 (2000), has no kinship with this case. Petitioner is not some observer "who has placed a wager upon the outcome." Gen. 18, quoting 529 U.S. at 772. This asserted royalty obligation is not "[a]n interest unrelated to injury in fact," or a "by-product" of a legal dispute. *Id.* at 772, 773. This *is* the legal dispute. Petitioner's payments under protest in response to Genentech's demands do not mean that petitioner is not injured. They demonstrate the opposite.

2. Genentech at one point suggests that petitioner and respondents do not have adverse legal interests. Gen. 15. That sort of argument was disposed of in *Aetna*, 300 U.S at 242 ("the parties had taken adverse positions with respect to their existing obligations . . . . an adjudication of present right upon established facts"). The very decision under review here acknowledges that "[l]icensor and licensee always have adverse legal interests . . . ." P.C.A. 8a (quotation marks omitted).

3. Genentech invokes, albeit in cloudy fashion, the ancient maxim of *volenti non fit injuria*, "wrong is not committed against one who consents."[5] It contributes nothing to the

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[5] See generally P. STEIN, REGULAE IURIS 148-49 (1966). The phrase came to be identified with the tort doctrine of assumption of risk. See

analysis, and it certainly does not overrule *Aetna, Maryland Casualty* and *Altvater*. Contracts are by their nature consensual, but that has never impeded resolution of disputes about unbreached contracts under the Declaratory Judgment Act.[6] Such disputes were a prominent reason for its enactment. See Pet. Br. 30. Indeed, declarations as to whether a contract may be terminated are one of the most common uses of the Act. 12 J. MOORE *et al.*, MOORE'S FEDERAL PRACTICE § 57.80 at 57-139 (3d ed. 2006). Petitioner never consented to pay royalties on an invalid patent, nor for non-infringing products. See pp. 10-11, *infra*. The patent on which Genentech demanded royalties did not even exist until four years after the license contract. And petitioner never promised not to sue. Moreover, *volenti non fit injuria* was a principle subject to overriding public policy;[7] the interest in patent challenges is the public's, not just a private party's. *E.g.*, *Cardinal Chemical*, 508 U.S. at 100.

4. Respondents' suggestion that jurisdiction should be declined for "prudential" reasons, Gen. 40, COH 32-34, 49-50, is far-fetched. Federal courts do not decline jurisdiction lightly, *Marshall* v. *Marshall*, 126 S. Ct. 1735, 1741 (2006), and patent validity and infringement are issues unquestionably assigned by statute to their jurisdiction. 28 U.S.C. § 1338(a). The patent laws regulate the interest in using ideas in the

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Warren, *Volenti Non Fit Injuria in Actions of Negligence*, 8 HARV. L. REV. 457, 459 (1895).

[6] Perhaps for that reason, Genentech asserts—in spite of the explicit contract count in the complaint, J.A. 136—that petitioner "is not seeking a declaration of rights under the terms of the parties' contract," Gen. 10. But the complaint expressly prayed for a declaration of rights under the license agreement. J.A. 147. Genentech acknowledged in the District Court that petitioner "seeks a declaration that it owes nothing under its license agreement with Genentech because its sales of Synagis® allegedly do not infringe any valid claim of the '415 patent." C.A.A. 2827.

[7] See RESTATEMENT (2D), TORTS § 496C(2)(1965); Friedmann, *Social Insurance and the Principles of Tort Liability*, 63 HARV. L. REV. 241, 251 (1949).

pubic domain that petitioner seeks to exercise. "Prudential standing," as explained in a case both respondents cite, encompasses "[1] the general prohibition on a litigant's raising another person's legal rights, [2] the rule barring adjudication of generalized grievances more appropriately addressed in the representative branches, and [3] the requirement that a plaintiff's complaint fall within the zone of interests protected by the law invoked." *Elk Grove Unified School Dist.* v. *Newdow*, 542 U.S. 1, 12 (2004), quoting *Allen* v. *Wright*, 468 U.S. 737, 751 (1984). None of those remotely fits here.

**B. *Ripeness.***

Respondents also challenge ripeness. Gen. 17, 21, 24-25, 31; COH 29-30. But the "primary purpose" of the Declaratory Judgment Act "was to enable persons to obtain a definition of their rights before an actual injury had occurred." *Steffel* v. *Thompson*, 415 U.S. 452, 478 (1974) (Rehnquist, J., concurring). It provides "an alternative to pursuit of . . . arguably illegal activity." *Id.* at 480. Ripeness here is apparent from three independent lines of well-established authority: (1) cases interpreting contracts before breach; (2) pre-enforcement interpretations of statutes and regulations; and (3) cases testing the validity of patents prior to any infringement.

1. The courts of appeals for decades under Article III and the Declaratory Judgment Act have adjudicated contract disputes—including patent-license disputes—without requiring breach, just as is contemplated in Fed. R. Civ. P. 57. See Pet. Br. 18-20, 33-34; Pet. Cert. 13-16. The disruption that would ensue if the Federal Circuit's view of Article III prevailed would affect commercial disputes of all kinds—especially insurance and contract disputes, which were a particular concern of the Declaratory Judgment Act. See Pet. Cert. 14-16, 21; Pet. Br. 13, 29.

2. Respondents acknowledge that a threat to enforce a law against one challenging it is "a *present* invasion" and "creates a ripe controversy regardless of whether the plaintiff complies with the law or defies it." COH 18 (emphasis in original).

The Act applies when "compliance is coerced by the threat of enforcement, and the controversy is both immediate and real." *Lake Carriers' Ass'n* v. *MacMullan*, 406 U.S. 498, 508 (1972). Here failure to pay royalties would risk not only contract damages but also liability for patent infringement, 35 U.S.C. § 271, which can carry statutory sanctions punitive in nature, 35 U.S.C. § 284. See *Avia Group Int'l, Inc.* v. *L.A. Gear Cal., Inc.*, 853 F.2d 1557, 1566 (Fed. Cir. 1988) (patent treble damages "deter willful patent infringement by punishing"); *Altvater*, 319 U.S. at 365 ("the involuntary or coercive nature of the exaction preserves the right . . . to challenge the legality of the claim").

3. From the first year of the Declaratory Judgment Act it was recognized that declaratory actions to test patent validity could be brought by parties who have produced an allegedly infringing product "or have actually prepared to produce such a device." *Jervis B. Webb Co.* v. *Southern Sys., Inc.*, 742 F.2d 1388, 1399 (Fed. Cir. 1984); see *Zenie Bros.* v. *Miskend*, 10 F. Supp. 779 (S.D.N.Y. 1935). Petitioner, of course, already manufactures and sells Synagis®, the allegedly infringing product.

4. Ripeness decisions usually address the timing of challenges to administrative rules or rulings, and in that context consider "the fitness of the issues for judicial decision and the hardship to the parties of withholding court consideration." *Abbott Labs.* v. *Gardner*, 387 U.S. 136, 149 (1967); see *National Park Hospitality Ass'n* v. *Department of Interior*, 538 U.S. 803, 808 (2003); *Public Serv. Comm'n* v. *Wycoff Co.*, 344 U.S. 237, 243 (1952) (prematurity a concern "especial[ly] in the field of public law"). Patent validity and infringement certainly are fit issues for judicial resolution; courts determine them all the time. The hardship on all parties, even on respondents, of not adjudicating the issue also is clear: either respondents stop receiving substantial royalty payments while petitioner risks the consequences of patent infringement, or petitioner continues to pay royalties on a patent which may be invalid, and if so by its existence harms

not just petitioner but the public as well. A breach of the license agreement would not make the record more precise.

Moreover, "the appropriate standard for determining ripeness of private party contract disputes is the traditional ripeness standard, namely, whether 'there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.'" *Principal Life Ins. Co.* v. *Robinson*, 394 F.3d 665, 671 (9th Cir. 2005), quoting *Maryland Casualty*, 312 U.S. at 273. This dispute is not about what respondents choose to call "facts that are hypothetical." COH 20. Adjudication does not require "powers of imagination." *Texas* v. *United States*, 523 U.S. 296, 301 (1998).[8]

5. Respondents argue that this record does not establish a sufficient controversy. But the allegations of the complaint are backed up with uncontroverted and documented declarations of conversations and correspondence reflecting a demand for royalties by Genentech and protest and apprehension of suit by petitioner. See J.A. 388 ("clear threat" of suit), 393, 419, 421, 426, 428, 431. Respondents have never denied that if petitioner stopped paying royalties, suit for patent infringement or breach of contract, or both, would follow.

**4. The License.**

1. Respondents scarcely mention the actual provisions of the license. This license contains no promise by petitioner not to sue. Genentech disclaims any warranty that the patent is valid. J.A. 411. And the license applies only to products that infringe a valid patent. J.A. 399, C.A.A. 3586.

Genentech complains that "MedImmune did not . . . negotiate any term that would permit it to initiate a judicial pro-

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[8] Analogy to the old equity bill of *quia timet*, see Gen. 22, does not advance this case. Indeed, *quia timet* would comfortably fit these circumstances: it protected parties from "future injury," *Borey* v. *National Union Fire Ins. Co.*, 934 F.2d 30, 32 (2d Cir. 1991), and was "generally used to prevent wrongs before they occurred." Raack, *A History of Injunctions in England Before 1700*, 61 IND. L.J. 539, 550 n.59 (1986).

ceeding challenging the validity of the patents while retaining the benefits of the license." Gen. 7. But nothing in the law says that subject-matter jurisdiction demands that a patent licensee must have obtained the licensor's permission to sue. And, by the same token, Genentech did not negotiate any term that would bar petitioner from suing, without termination, to invalidate the patent—even though the record shows that in other licenses Genentech has done precisely that, obtaining (in spite of *Pope Mfg. Co.* v. *Gormully*, 144 U.S. 224, 235 (1892), and *Lear*) the licensee's promise not to challenge validity. C.A.A. 1702, referenced J.A. 274. Genentech's reasoning would imply a ban on challenging patent validity into every license contract, and even a ban on federal subject-matter jurisdiction as well.

2. Respondents argue that a license should be treated as if it were a settlement of a lawsuit. But it is not, and even if it were, a settlement agreement would be a defense on the merits, not a bar to federal subject-matter jurisdiction. "[A]bsence of a valid . . . cause of action does not implicate subject-matter jurisdiction." *Steel Co.* v. *Citizens for a Better Environment*, 523 U.S. 83, 89 (1998). Also, if a settlement agreement contained a provision prohibiting a patent challenge, it would be unenforceable as contrary to *Lear*. Pet. Br. 37; *Business Forms Finishing Serv., Inc.* v. *Carson*, 452 F.2d 70, 73-75 (7th Cir. 1971) (Stevens, J.); *Kraly* v. *National Distillers & Chem. Corp.*, 502 F.2d 1366, 1369 (7th Cir. 1974); *but see Flex-Foot, Inc.* v. *CRP, Inc.*, 238 F.3d 1362, 1368 (Fed. Cir. 2001).

3. Moreover, to transmute a license into a litigation settlement is an unsupportable stretch. The law for centuries has defined a license, not as a settlement of a dispute, but as "[a] permission, usu[ally] revocable, to commit some act that would otherwise be unlawful." BLACK'S LAW DICTIONARY 938 (8th ed. 2004). A lease on an apartment or house is not a settlement of a trespass claim by the landlord. A lease dispute meets the standards of Article III and the Declaratory Judgment Act even when the tenant has not committed a

breach. *118 East 60th Owners, Inc.* v. *Bonner Properties, Inc.*, 677 F.2d 200, 202 n.1 (2d Cir. 1982); Pet. Br. 19-20. The license in this case specifically did not resolve the validity of any patent. J.A. 411. The patent, indeed, was not issued (and then under very unusual circumstances) until four years after the license. See J.A. 509; Pet. Br. 4-6.

4. Even if licenses were private settlements, the interests in an action challenging patent validity are not purely private. Also at stake is restoration of public ideas to the public domain. For that reason there is a strong federal policy favoring patent challenges. See Pet. Br. 13, 35; *Cardinal Chemical*, 508 U.S. at 100 (validity of patent should be determined even after determination that product did not infringe).[9]

**5. "Settled Expectations."**

Respondents say that to reverse the Federal Circuit would upset "settled expectations." COH 12. That is demonstrably not so.

1. For nearly a year after this case was filed, neither respondent moved to dismiss for lack of subject-matter jurisdiction. They did not do so until the Federal Circuit issued *Gen-Probe*; then they did so at once. There was indeed, as the district court in *Gen-Probe* called it, "settled law," see Pet. Br. 40 & n.16—and it was settled the opposite way, including in one of the Federal Circuit's first and leading decisions, *C.R. Bard, Inc.* v. *Schwartz*, 716 F.2d 874 (Fed. Cir. 1983)—whose authority the District Court, like the district court in *Gen-Probe*, pointed out, P.C.A. 30a, but which respondents' briefs scarcely acknowledge.[10]

2. The fact is, *Gen-Probe* was a shock that took both the bench and the bar by surprise. In *Gen-Probe* itself, the issue did not come up until two years into the case, when after

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[9] One respondent maintains that "the only substantive rights created by Congress belong to Respondents;" it contends also that "any potential justiciable controversy is either moot or unripe." COH 25, 28.

[10] Genentech mentions *C.R. Bard* once in a footnote, Gen. 34 n.25; City of Hope does not acknowledge it at all.

losing at trial, the *Gen-Probe* patentee moved to dismiss for lack of subject-matter jurisdiction. The district court there emphatically denied the motion, as contrary to "settled law," see Pet. Br. 40, but the Federal Circuit announced the new *Gen-Probe* constitutional doctrine. In *Centocor* yet another district court denied such a jurisdictional objection—then reversed itself after *Gen-Probe*. See Pet. Br. 40.

3. Treatise-writers and scholars shared the same understanding. *E.g.*, B. BRUNSVOLD & D. O'REILLEY, DRAFTING PATENT LICENSE AGREEMENTS 167 (5th ed. 2004) (licensee has "freedom to contest the validity of the licensed patent at any time"); McCarthy, *"Unmuzzling" the Patent Licensee*, 59 J. PAT. OFF. SOC'Y 544, 554 (1977) ("consistent with the purposes of declaratory judgments" and more desirable than breach); Fisher, *The Licensee's Choice*, 6 TEXAS INTELL. PROP. L.J. 1, 12 (1997) (citing *C.R. Bard*); 12 J. MOORE *et al.*, § 57.22[8][c][i] at 57-80 ("licensee need not terminate the license in order to maintain a federal declaratory relief action for patent invalidity," citing *inter alia C.R. Bard*).[11]

**6. *Lear* and Licensee Estoppel.**

1. It is remarkable that Genentech opens its brief by citing *Kinsman* v. *Parkhurst*, 18 How. 289 (1856), the very case identified by this Court as having established the doctrine of licensee estoppel, *Lear*, 395 U.S. at 663—which *Lear* explicitly overruled. *Id.* at 671. And the same brief closes by urging a return to "[t]he traditional understanding that a license resolves any cognizable dispute over the validity of the patent" if the license is in place. Gen. 50.

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[11] Respondents argue that *Gen-Probe* somehow was foreshadowed in *Studiengesellschaft Kohle m.b.H.* v. *Shell Oil Co.*, 112 F.3d 1561 (Fed. Cir.), *cert. denied*, 522 U.S. 996 (1997), a case that did not concern federal subject-matter jurisdiction (but did have dicta severely critical of *Lear*). 112 F.3d at 1567. Neither respondent cited the case in the Court of Appeals, and it was barely mentioned in *Gen-Probe*. See Gen. 35 n.25, COH 6, 49; 359 F.3d at 1381.

That might have been the "traditional understanding" *prior to Lear*. Respondents repeatedly seek authority in Nineteenth-Century decisions of this Court that, indeed, may have reflected the law once upon a time, but were explicitly rejected in *Lear*. *E.g.*, Gen. 7, COH 35, 49, relying on *United States* v. *Harvey Steel Co.*, 196 U.S. 310 (1905), a case particularly criticized in *Lear*, 395 U.S. at 664. City of Hope invokes "the centuries-old equitable rule of licensee estoppel," COH 11, and praises the Federal Circuit's "reaffirmation of the historical scope of licensee estoppel," *id.* 50. Some of respondents' *amici* urge that "the Court should overrule or clarify *Lear v. Adkins*." Donaldson Br. 1.[12]

2. Licensee estoppel, even if it were still a permitted defense, is not and never was a *jurisdictional* defense.

3. Both respondents complain that declaratory relief would allow petitioner to "have its cake and eat it too." Gen. 43; COH 47-48. The same was argued unsuccessfully in *Lear*. The same might just as easily be said of the innumerable contract declaratory-judgment cases brought without breach; see, *e.g.*, Fed. R. Civ. P. 57 advisory comm. note; Pet. Br. 33. Moreover, the situation is not at all one-sided. Genentech is continuing to obtain the royalties called for in the license. Petitioner is providing the very income stream that patent owners say is so important to them. See Columbia Br. 4.

This Court in *Lear* considered and rejected such pleas of unfairness. "[T]he equities of the licensor do not weigh very heavily when they are balanced against the important public interest in permitting full and free competition in the use of ideas which are in reality a part of the public domain." *Lear*, 395

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[12] One respondent even accuses the *Lear* opinion of "confusion" and of having "misread several cases it relied on," as well as of "one-sidedness." COH 37, 38 n.19, 41. It is unusual for *Lear*'s author to be faulted on judicial craftsmanship or evenhandedness. *Cf.* Friendly, *Mr. Justice Harlan, as Seen by a Friend and Judge of an Inferior Court*, 85 HARV. L. REV. 382, 384 (1971) ("there has never been a Justice of the Supreme Court who has so consistently maintained a high quality of performance").

U.S. at 670. "[I]t does not seem to us to be unfair to require a patentee to defend the Patent Office's judgment when his licensee places the question in issue . . . ." *Id.* See also *Kewanee Oil Co.* v. *Bicron Corp.*, 416 U.S. 470, 488-89 (1974).

**7. Discretion.**

Respondents now argue, for the first time in this litigation, that if subject-matter jurisdiction exists, this Court nevertheless should hold that declaratory relief must be denied as a matter of discretion. Gen. 41, COH 32.

1. Respondents concede, Gen. 40, COH 49, that this new prayer was not decided or even raised in either the District Court or the Federal Circuit, and was not mentioned in respondents' brief in opposition to certiorari. Hence no record to support (or oppose) such a ruling was made. "While it is true that a respondent may defend a judgment on alternative grounds, we generally do not address arguments that were not the basis for the decision below." *Matsushita Elec. Indus. Co.* v. *Epstein*, 516 U.S. 367, 379 n.5 (1996); see also *Ponte* v. *Real*, 471 U.S. 491, 500 (1985). "Prudence . . . dictates awaiting . . . developed arguments on both sides and lower court opinions squarely addressing the question." *Yee* v. *City of Escondido*, 503 U.S. 519, 538 (1992).

2. The District Court was precluded from exercising discretion by the Federal Circuit's announcement in *Gen-Probe* that district courts absolutely lack Article III jurisdiction in such cases, a ruling which the District Court despite "serious misgivings" obeyed. P.C.A. 30a-31a. The appellate exercise of discretion that respondents now ask for would be contrary to longstanding practice in declaratory-judgment cases. Such exercise of discretion is committed in the first instance to the district court. *E.g.*, *Brillhart* v. *Excess Ins. Co.*, 316 U.S. 491, 498 (1942). Discretion, of course, "is not whim," *Martin* v. *Franklin Capital Corp.*, 126 S.Ct. 704, 710 (2005), but it is not applied initially by appellate courts:

> "We believe it more consistent with the [declaratory judgment] statute to vest district courts with discretion in

> the first instance, because facts bearing on the usefulness of the declaratory judgment remedy, and the fitness of the case for resolution, are peculiarly within their grasp."

*Wilton* v. *Seven Falls Co.*, 515 U.S. 277, 289 (1995), discussed at Pet. Br. 44. *Cf.* also *Cardinal Chemical*, 508 U.S. at 102-103 (remanding for discretion to be exercised); *id.* at 103 (Scalia, J., concurring in part and in judgment) ("failure to exercise *any discretion at all*") (emphasis in original).[13]

3. Respondents seek a categorical rule that even if there is Article III subject-matter jurisdiction, declaratory judgments of patent validity must always be held an abuse of discretion when the licensee is not in breach. Gen. 41, COH 32-33. But "[t]he lower federal courts ought not to be narrowly confined in determining whether a declaratory judgment is an appropriate remedy under all the circumstances." *Altvater*, 319 U.S. at 370 (opinion of Frankfurter, J.). Just last Term in *eBay, Inc.* v. *MercExchange, L.L.C.*, 126 S. Ct. 1837, 1841 (2006), a case addressing equitable relief,[14] this Court underscored the very point:

> "Just as the District Court erred in its categorical denial of injunctive relief, the Court of Appeals erred in its categorical grant of such relief."

This Court unanimously vacated and remanded "so that the District Court may apply that [traditional equity four-factor] framework in the first instance." *Id.* Four Justices further emphasized that "courts should apply the well-established,

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[13] See also *Maryland Cas. Co.* v. *United Corp.*, 111 F.2d 443, 446 (1st Cir. 1940) (Magruder, J.) ("Since the complaint was dismissed on the mistaken ground of lack of jurisdiction, the judgment appealed from should not be affirmed, even if there existed adequate grounds on which the complaint might have been dismissed as a matter of discretion.").

[14] Respondents often elide the distinction between equitable discretion and discretion under the Declaratory Judgment Act. There can be "critical distinctions which make declaratory relief appropriate where injunctive relief would not be." *Steffel*, 415 U.S. at 581 (Rehnquist, J., concurring). See also, *e.g.*, *Maryland Casualty*, 312 U.S. at 274 (denying injunction but granting declaratory judgment).

four-factor test—without resort to categorical rules." *Id.* at 1842 (Kennedy, J., concurring).

4. Apparently under cloak of their equity analogies,[15] respondents' briefs are laced with denunciations of petitioner for having filed this lawsuit. Probably licensees who challenge patents are not likely to be popular with patent owners. One respondent recites "duplicitous," "duplicity," "duplicitously." Gen. 8, 42, 43; see also Qualcomm Br. 8, 9, 10 ("treachery" "duplicity," "perfidy"); Colum. Br. 2, 5 ("pernicious").[16]

Respondents describe this litigation as "license and then sue." Gen. 42; COH 8 n.4. But overlap of biotechnology patents makes widespread licensing a necessity for new products. In fact, petitioner, to remove any doubt that it could legally develop and market Synagis®, took licenses under nearly two dozen other patents besides the one at issue; the validity of only one of those is under challenge. See *MedImmune, Inc.* v. *Centocor, Inc.*, No. 05-656. The license here was agreed to in 1997; the patent at issue did not come into existence until late 2001; this action was filed in 2003.

Petitioner has continued to pay royalties and do business with Genentech, including negotiating later license agreements under the patent for other products. Respondents now call that "inequitable." Gen. 43; see COH 7. But those later licenses are not at issue here, nor are they relevant to federal subject-matter jurisdiction. And both parties well knew that their dispute as to Synagis® remained unresolved; they discussed both the present dispute and the later licenses in the same letters. See, *e.g.*, J.A. 426, 429, 431, 433-35. Respondents ignore that

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[15] If equities were to be balanced, Genentech's facially extraordinary conduct in obtaining the patent would certainly need to be explored and considered. See Pet. Br. 4-6.

[16] Severe denunciation apparently is frequent in contemporary biotechnology litigation. City of Hope in a pending case accuses Genentech of "cheating and deception." City of Hope's Answer Brief, *City of Hope Nat'l Med. Ctr.* v. *Genentech, Inc.*, No. S129463, S. Ct. Cal. (Sept. 19, 2005) at 63; see also *id.* at 102 ("Genentech stonewalled, lied, and cheated"); 103 ("trickery" "deceit").

a prominent stated purpose of the Declaratory Judgment Act was to encourage parties to continue their ongoing commercial relationships, allowing particular disputes to be resolved judicially *without* breaches of contract. See Pet. Br. 29-31.

Petitioner submits that it has respected the letter and purpose of the patent laws. Petitioner did not resort to a breach of contract, which not only would have put petitioner in jeopardy, but also would have deprived Genentech of substantial royalties and, if the patent were upheld, could have led to an injunction that would take a unique life-saving medicine for infants off the market.

**8. Practical Consequences.**

1. Any public or commercial benefit from reinterpreting the Constitution, forcing licensees to escalate validity disputes into high-stakes patent-infringement litigation, is difficult to discern. Respondents show none—unless it were considered beneficial to make patent validity challenges less frequent and far more dangerous. Up to now, however, federal patent policy, recognized by this Court, has been to "*encourage* authoritative testing of patent validity." *Blonder-Tongue Labs.* v. *University of Ill. Found.*, 402 U.S. 313, 344 (1971) (emphasis supplied). Congress has shown no inclination to change that. That has also been the view endorsed by the Executive Branch for decades,[17] as it is once again here. See Brief for the United States as *Amicus Curiae* Supporting Petitioner (reflecting views of Patent and Trademark Office, the National Institutes of Health, and other federal agencies) 1-2, 27; FTC, TO PROMOTE INNOVATION (2003) (cited in *eBay*, 126 S. Ct. at 1842 (Kennedy, J., concurring)); Pet. Br. 36, 45-48.

2. Some *amici* prophesy, if the Federal Circuit's new doctrine is reversed, "thousands, even millions, of licensees" filing suits against patent holders. Qualcomm Br. 11. One

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[17] *E.g.*, Brief for the United States as *Amicus Curiae*, *Lear, Inc.* v. *Adkins*, No. 56, OT 1968 (Oct. 25, 1968) at 23 ("The patentee is not a victim of unfair dealing merely because his licensee challenges the patent.").

even surprisingly predicts that licensees will do so "no matter whether the case for invalidity is strong or weak." Boston PLA Br. 19. No evidence supports such speculation. As others recognize, "patent litigation is notoriously expensive," Allison Br. 8, "enormously expensive," 3M Br. 12; see *Blonder-Tongue*, 402 U.S. at 334; Pet. Br. 45. No one has claimed that any flood of lawsuits occurred after *Lear*.

3. Just as unsupported are lamentations that if licensees once again may sue without breach, patentees might stop issuing licenses. But licenses are how patentees make money. "[A] large part of [a patent's] value consists in the profits derived from royalties and license fees." *Waterman* v. *Mackenzie*, 138 U.S. 252, 260 (1891). "[L]icensing fees are among the most important rewards that a patent owner garners from a valid patent." Qualcomm Br. 24. Licensing did not stop after *Lear*, and licenses have been granted by the thousands under the pre-*Gen-Probe* law.

Likewise, to predict that licenses might cost more, Gen. 47, COH 44, is entire speculation. Royalty rates are a product of bargaining power and market forces.[18] At least as likely, concern about validity challenges would cause patentees to charge less, especially for weak patents, calculating that licensees who pay less are less motivated to mount expensive challenges. And, of course, to the extent invalid patents would no longer distort the market, prices to consumers would tend to fall, and innovation rise.

4. Finally, the desirability or utility of demanding contract breaches and unauthorized infringement before resolving dis-

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[18] Respondents insist, without evidence and without explanation of relevance, that this license came at bargain rates. Gen. 6, 28, 43, 48-49; COH 5, 34. But rates presumably reflect market forces. "A patent empowers the owner to exact royalties as high as he can negotiate . . . ." *Brulotte* v. *Thys Co.*, 379 U.S. 29, 33 (1964). There is no evidence that Genentech behaved any differently.

putes is not self-evident.[19] It certainly was not what was intended by those who advocated and adopted the Declaratory Judgment Act. See Pet. Br. 29-31. And Congress does not treat infringement as blameless. Patent infringement often carries punitive sanctions of treble damages. *E.g.*, 35 U.S.C. § 284 (treble damages for willful patent infringement); see also 17 U.S.C. § 506 (criminal penalties for willful copyright infringement).

Any rule that would substantially discourage patent challenges by the parties most knowledgeable and motivated to bring them, see *Lear*, 395 U.S. at 670, by escalating the cost and risk of doing so, is contrary to the purpose of the patent laws as emphatically and repeatedly held by this Court. *E.g.*, *Lear; Blonder-Tongue; Cardinal Chemical.* "[S]ometimes *too much* patent protection can impede rather than 'promote the Progress of Science and useful Arts'. . . ." *Laboratory Corp.* v. *Metabolite Labs., Inc.*, 126 S. Ct. 2921, 2922 (2006) (Breyer, J., dissenting from dismissal) (emphasis in original). Just as "[t]he Fourteenth Amendment does not enact Mr. Herbert Spencer's Social Statics," *Lochner* v. *New York*, 198 U.S. 45, 75 (1905) (Holmes, J., dissenting), so Article III did not build into the Constitution the barrier to patent challenges that respondents advocate.

## CONCLUSION

For the reasons stated herein and previously, the judgment should be reversed.

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[19] "The inviolability of contracts, and the duty of performing them, as made, are foundations of all well-ordered society . . . ." *Murray* v. *Charleston*, 96 U.S. 432, 449 (1877). *Compare* Holmes, *The Path of the Law*, 10 HARV. L. REV. 457, 462 (1897) (breach of contract not a moral issue), *with* C. FRIED, CONTRACT AS PROMISE: A THEORY OF CONTRACTUAL OBLIGATION 16 (1981) ("[a]n individual is morally bound to keep his promises . . . ."); see Sharp, *Pacta Sunt Servanda*, 41 COLUM. L. REV. 783 (1941).

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No. 05-608

# In the Supreme Court of the United States

MEDIMMUNE, INC., PETITIONER

*v.*

GENENTECH, INC., ET AL.

*ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT*

## BRIEF FOR THE UNITED STATES AS AMICUS CURIAE SUPPORTING PETITIONER

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## QUESTION PRESENTED

Whether Article III's grant of jurisdiction of "all Cases * * * arising under * * * the Laws of the United States," implemented in the "actual controversy" requirement of the Declaratory Judgment Act, 28 U.S.C. 2201(a), requires a patent licensee to refuse to pay royalties and commit material breach of the license agreement before suing to declare the patent invalid, unenforceable, or not infringed.

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# In the Supreme Court of the United States

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## BRIEF FOR THE UNITED STATES AS AMICUS CURIAE SUPPORTING PETITIONER

### INTEREST OF THE UNITED STATES

This case presents the question whether a patent licensee in good standing may challenge the validity and scope of the licensed patent in federal court. The United States Patent and Trademark Office (PTO or Patent Office) is responsible for "the granting and issuing of patents," 35 U.S.C. 2(a), as well as for advising the President on domestic and international issues of patent policy, 35 U.S.C. 2(b)(8). Several federal agencies, including in particular the National Institutes of Health, are extensively engaged in the licensing of patented inventions to private entities, and the United States is also a licensee of various patents. In addition, this case implicates core concerns of the Federal Trade Commission and the Antitrust Division of the United States Depart-

ment of Justice, because intellectual property licensing can enhance consumer welfare by allowing for the efficient exploitation of intellectual property, but the existence of invalid patents in the marketplace can impede efficient licensing, hinder competition, and undermine incentives for innovation.[1] The government accordingly has a substantial interest in this Court's resolution of the question presented.

## STATEMENT

1. The federal Declaratory Judgment Act (the Act) provides that "[i]n a case of actual controversy within its jurisdiction," any court of the United States "may declare the rights and other legal relations of any interested party," without regard to whether "further relief is or could be sought." 28 U.S.C. 2201(a); see Fed. R. Civ. P. 57. Integral to the Declaratory Judgment Act is the requirement of an "actual controversy." For years prior to Congress's adoption of the Act, "there were responsible expressions of doubt that constitutional limitations on federal judicial power would permit any federal declaratory judgment procedure." *Public Serv. Comm'n* v. *Wycoff Co.*, 344 U.S. 237, 241 (1952). In 1933, how-

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[1] See generally Federal Trade Comm'n, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy* (2003) (*FTC Innovation Report*), *available at* <http:// www.ftc.gov/os/2003/10/innovationrpt.pdf> (last visited May 11, 2006); U.S. Dep't of Justice & Federal Trade Comm'n, *Antitrust Guidelines for the Licensing of Intellectual Property* (1995) (*DOJ/FTC Licensing Guidelines*), *reprinted in* 4 Trade Reg. Rep. (CCH) ¶ 13,132, at 20,733 (1995), *available at* <http://www.usdoj.gov/atr/public/guidelines/0558.pdf> (last visited May 11, 2006); see also U.S. Dep't of Justice, *Report of the Department of Justice's Task Force on Intellectual Property* (200-), *available at* <http://www.usdoj.gov/olp/ip_task_force_report.pdf> (last visited May 11, 2006).

ever, this Court held that a declaratory judgment action arising from the Tennessee state courts presented a justiciable case or controversy. *Nashville, Chattanooga & St. Louis Ry.* v. *Wallace*, 288 U.S. 249, 264-265 (1933). The *Wallace* Court emphasized that, notwithstanding the absence of a claim for injunctive or other coercive relief, the case presented a concrete legal dispute "of the kind which this court traditionally decides." *Id.* at 262. The "declaratory" nature of the remedy sought did not render the case nonjusticiable under Article III: "[T]he Constitution does not require that the case or controversy should be presented by traditional forms of procedure, invoking only traditional remedies. The judiciary clause of the Constitution defined and limited judicial power, not the particular method by which that power might be invoked." *Id.* at 264.

Congress enacted the Declaratory Judgment Act in the following year. See *Wycoff*, 344 U.S. at 241-242. The Senate committee report explained that the *Wallace* decision had dissipated the prevailing confusion between declaratory judgments and impermissible advisory opinions. See S. Rep. No. 1005, 73d Cong., 2d Sess. 5 (1934). Thus, "[t]he Federal bill specifically provides for declaratory adjudication only 'in cases of actual controversy.' That precludes hypothetical, academic, or moot cases. The words 'in cases of actual controversy' are designed to make certain what would be obvious even without them." *Ibid.*

This Court subsequently upheld the constitutionality of the Declaratory Judgment Act, highlighting both the breadth of the remedy thereby created and the limitations imposed by Article III on its administration: "The Declaratory Judgment Act must be deemed to fall within th[e] ambit of congressional power, so far as it

authorizes relief which is consonant with the exercise of the judicial function in the determination of controversies to which under the Constitution the judicial power extends." *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227, 240 (1937).

2. a. Petitioner MedImmune, Inc., is a biotechnology company whose principal product is Synagis®, a drug used in the prevention of respiratory tract disease in infants. Pet. App. 21a. In 1997, petitioner entered into a patent license agreement with respondents Genentech, Inc., a biotechnology company, and City of Hope, a nonprofit organization. *Id.* at 4a, 21a-22a, 28a-29a. That license agreement covered, among other things, a then-pending patent application, which eventually matured into U.S. Patent No. 6,331,415 (Cabilly II patent). *Id.* at 4a, 28a.[2]

In December 2001, the PTO issued the Cabilly II patent, which was assigned to respondents. Pet. App. 3a-4a, 21a-22a.[3] Shortly thereafter, respondents in-

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[2] The Cabilly II patent is a continuation of respondents' Cabilly I patent, which the license agreement also covered. Pet. App. 2a.

[3] In 1990, the PTO declared an "interference" proceeding between the then-pending Cabilly II application and U.S. Patent No. 4,816,397 (Boss patent), which was owned by CellTech R&D, Ltd. Pet. App. 2a. In 1998, petitioner separately entered into a license agreement with CellTech for rights to the Boss patent. *Id.* at 4a. By obtaining licenses from both CellTech and respondents, petitioner ensured that it would have enforceable license rights irrespective of which side prevailed in the interference proceeding. Also in 1998, the PTO decided that the Boss patent had priority and administratively cancelled respondents' Cabilly II application. *Cabilly* v. *Boss*, 55 U.S.P.Q. 2d (BNA) 1238 (BPAI 1998). After respondents challenged that determination in federal court, they entered into a settlement agreement with Celltech which provided that the Cabilly II application was entitled to priority over the Boss

formed petitioner that they believed Synagis® was covered under the patent and, consequently, that sales of Synagis® were subject to royalties under the parties' 1997 license agreement. *Id.* at 4a. Petitioner initially denied that Synagis® infringed the Cabilly II patent, but soon began paying the demanded royalties, informing respondents that its payments were made "under protest and with reservation of all of our rights." J.A. 426; see J.A. 133. Petitioner maintains that it has continued to pay royalties and otherwise remain in good standing under its license agreement only to avoid the risk of an infringement action by respondents to enjoin sales of Synagis®, which petitioner claims accounts for over 80% of its revenues. J.A. 386-389. In 2003, petitioner filed this action for a declaratory judgment that the Cabilly II patent is invalid, unenforceable, and not infringed by Synagis®. Pet. App. 4a, 22a.

b. The district court dismissed petitioner's complaint for lack of jurisdiction based on the Federal Circuit's then-recent decision in *Gen-Probe Inc.* v. *Vysis, Inc.*, 359 F.3d 1376, cert. dismissed, 543 U.S. 941 (2004). See Pet. App. 28a-31a. In *Gen-Probe*, the Federal Circuit applied its two-part test for determining whether there is an "actual controversy" under the Declaratory Judgment Act in patent cases, the first prong of which

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patent. In return, Celltech obtained the right to share in all royalties that respondents received on the Cabilly II application and any resulting patents. The parties' settlement was conditioned on issuance of a court order vacating PTO's cancellation of the Cabilly II application and directing PTO to issue the Cabilly II patent. J.A. 334-335. At the joint request of the parties, the district court issued an order and entered judgment to that effect. J.A. 343-348. After further proceedings before the PTO, the PTO issued the Cabilly II patent. Pet. App. 3a-4a.

requires that the declaratory judgment plaintiff must labor under "a reasonable apprehension * * * that it will face an infringement suit." 359 F.3d at 1380.[4] *Gen-Probe* held that, as a matter of law, a patent licensee in good standing cannot establish an "actual controversy" with the patent owner, because the license agreement itself "obliterate[s] any reasonable apprehension of a lawsuit." *Id.* at 1381. Although the district court in this case suggested that it harbored "serious misgivings" about the wisdom of the *Gen-Probe* rule, it discerned "no relevant facts that distinguish this case" and concluded that it had no choice but to dismiss. Pet. App. 31a.[5]

3. The court of appeals affirmed, concluding that *Gen-Probe* was dispositive of the question of justiciability. Pet. App. 1a-9a.[6] The court of appeals distinguished *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969), on the ground

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[4] The Federal Circuit's two-part test requires "both (1) an explicit threat or other action by the patentee, which creates a reasonable apprehension on the part of the declaratory judgment plaintiff that it will face an infringement suit, and (2) present activity which could constitute infringement or concrete steps taken with the intent to conduct such activity." *Gen-Probe*, 359 F.3d at 1380 (quoting *BP Chems. Ltd.* v. *Union Carbide Corp.*, 4 F.3d 975, 978 (Fed. Cir. 1993)).

[5] The district court also rejected on the merits petitioner's antitrust claims, which included a claim that the interference settlement between respondents and Celltech (see note 3, *supra*) was collusive and fraudulent. See Pet. App. 22a; see also *id.* at 9a-15a.

[6] The Federal Circuit also rejected petitioner's remaining contentions on appeal, including a variety of challenges to the district court's disposition of petitioner's antitrust claims. Pet. App. 9a-17a. Those other issues are not before this Court. Judge Clevenger dissented from aspects of the court's holding on those remaining issues, but joined in full the court's dismissal of petitioner's declaratory judgment claims under the *Gen-Probe* rule. See *id.* at 17a-20a.

that "this case does not raise the question of whether patent invalidity is available as a defense to suit against a defaulting licensee—the licensee estoppel theory that was laid to rest in *Lear*—for there is no defaulting licensee and no possibility of suit." Pet. App. 6a. Rather, the court reasoned, "the issue here is not one of estoppel, but of availability of the declaratory judgment procedure." *Ibid.* In reaffirming the *Gen-Probe* rule, the court of appeals concluded that allowing petitioner to sue would "distort[] the equalizing principles that underlie the Declaratory Judgment Act." *Id.* at 7a. If petitioner's interpretation of the "actual controversy" requirement were to prevail, the Federal Circuit reasoned, the patentee, having contracted away its right to sue for infringement, would find itself "in continuing risk of attack on the patent whenever the licensee chooses—for example, if the product achieves commercial success—while the licensee can preserve its license and royalty rate if the attack fails." *Ibid.*[7]

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[7] During the pendency of this case, a request was filed with the PTO for ex parte reexamination of the Cabilly II patent. See generally 35 U.S.C. 301 *et seq.* PTO reexamination is an administrative proceeding that may, but need not, result in the limitation or cancellation of some or all of the claims in a patent. See 35 U.S.C. 301-307 (2000 & Supp. III 2003) (ex parte reexaminations); see also 35 U.S.C. 311-318 (2000 & Supp. III 2003) (inter partes reexaminations). PTO granted the request and, in September 2005, provisionally rejected all of the claims of the Cabilly II patent as invalid for "obviousness-type double-patenting." *Patent of Cabilly*, Application No. 90/007,542, at 2-3 (PTO Sept. 13, 2005), *available in* Public PAIR (PTO); see *In re Berg*, 140 F.3d 1428, 1431-1432 (Fed. Cir. 1998) (explaining that "obviousness-type double patenting" is a judge-made doctrine that requires "rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent" in order "to prevent an unjustified extension of the term of the right

## SUMMARY OF ARGUMENT

The Federal Circuit has adopted a restrictive test to determine the existence of an "actual controversy" in declaratory judgment cases that categorically precludes licensees in good standing from challenging patents under which they are licensed. Nothing in Article III, the Declaratory Judgment Act, or this Court's cases warrants such a special rule of justiciability for patent cases.

This Court has consistently held that whether a complaint alleges an "actual controversy" for purposes of the Declaratory Judgment Act presents a fact-sensitive issue that requires case-by-case determination. The question in each case essentially turns on whether the parties are involved in a substantial controversy that is sufficiently concrete and real that the court can resolve it through declaratory relief. When a plaintiff requests a declaration based on generalized facts and abstract legal claims, an actual controversy is lacking. But when the parties are truly adversarial, and the dispute is factually and legally concrete such that the requested declaration will definitely resolve a specific dispute, a justiciable controversy is present.

In patent cases, however, the Federal Circuit has "synthesi[zed]" this Court's contextual approach into a two-part test, which the court of appeals rigidly applies. Pet. App. 7a; *Gen-Probe Inc.* v. *Vysis, Inc.*, 359 F.3d 1376, 1379-1382, cert. dismissed, 543 U.S. 941 (2004). Under that test, a declaratory judgment plaintiff must

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to exclude granted by a patent by allowing a second patent claiming an obvious variant of the same invention to issue to the same owner later"). The reexamination of the Cabilly II patent remains pending before the PTO.

have a "reasonable apprehension" of a suit for infringement by the patentee before a justiciable "case or controversy" will be recognized. In the court of appeals' view, therefore, a licensee in good standing cannot, as an Article III matter, challenge a patent under which it is licensed because the licensee can have no reasonable apprehension of an infringement suit.

That limitation on the availability of declaratory relief cannot be squared with this Court's cases or with the congressional purposes underlying the Act. As demonstrated by decisions of this Court involving pre-enforcement challenges to statutes, it is sufficient for a declaratory judgment plaintiff to demonstrate a genuine risk of enforcement and a reasonable likelihood that he would engage in the proscribed conduct if the threat were removed. A declaratory judgment plaintiff need not run the risks entailed in actually violating the law in order to make out an "actual controversy." See, *e.g.*, *Steffel* v. *Thompson*, 415 U.S. 452, 459, 475 (1974). Indeed, this Court has already rejected the proposition that a licensee's ongoing payment of patent royalties negates any justiciable dispute over the validity of the patent. *Altvater* v. *Freeman*, 319 U.S. 359 (1943). Yet the Federal Circuit's insistence on compliance with its two-part test requires a patent licensee to commit a material breach of its license agreement in order to create an "actual controversy." That result is contrary to the congressional purposes behind the Act, which was adopted to free parties of the requirement that they act at their peril on their own interpretation of their rights before being able to obtain a judicial construction of those rights.

Under a proper interpretation of the Declaratory Judgment Act, this case presents an "actual contro-

versy." Petitioner claims that respondents' Cabilly II patent is invalid and not infringed. Absent respondents' patent, and their claim that petitioner's principal product infringes that patent, petitioner would not be paying royalties to respondents on its sales of that product. The dispute between the parties is concrete, specific, and susceptible of judicial resolution, and the federal courts can therefore resolve it. The fact that the litigants have entered into a license agreement, under which petitioner currently is paying royalties, is simply not significant for Article III purposes, except to the extent that petitioner's payment of royalties provides concrete proof of the extent of the parties' dispute.

The court of appeals erred in suggesting that its judgment is supported by federal patent policy. Most fundamentally, policy considerations could not justify a departure from traditional Article III principles. In any event, considerations of patent policy actually point in favor of allowing licensees in good standing to challenge the validity of patents. Many patents are clearly valid and will not be subjected to challenge by licensees. But some patents are invalid, and there is a strong federal policy, as this Court has repeatedly recognized, in ridding the economy of such patents. Licensees, moreover, are often the sole or principal parties with the requisite knowledge and incentive to challenge them. And patent owners are far from defenseless; they have been granted a valuable legal monopoly, backed by a statutory presumption of validity and the threat of powerful legal remedies. It is not inequitable to force a patent holder to defend its patent.

## ARGUMENT

### A PATENT LICENSEE NEED NOT BREACH ITS LICENSE AGREEMENT IN ORDER TO ESTABLISH AN "ACTUAL CONTROVERSY" UNDER ARTICLE III OR THE DECLARATORY JUDGMENT ACT

Under the interpretation of the Declaratory Judgment Act adopted by the Federal Circuit in *Gen-Probe*, *supra*, and applied below, a patent licensee in good standing cannot bring a declaratory judgment action to challenge the patent under which it is licensed. That restrictive rule has no basis in Article III, the Declaratory Judgment Act, or this Court's jurisprudence. Under settled legal principles, the fact that a licensee is in good standing does not prevent the existence of an Article III "case or controversy" between the licensee and the patent holder with respect to the validity or construction of a licensed patent. And because the "actual controversy" requirement of the Declaratory Judgment Act authorizes declaratory relief in all cases and controversies cognizable under Article III, *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227, 241 (1937), the Act leaves no room for the creation of heightened obstacles to justiciability that apply only in actions under the federal patent laws.

#### A. The "Actual Controversy" Inquiry Entails A Fact-Sensitive, Case-By-Case Examination Of The Concreteness And Reality Of The Asserted Controversy

1. This Court has made clear that the determination whether an "actual controversy" exists for purposes of the Declaratory Judgment Act necessarily entails a fact-sensitive, case-by-case inquiry. As the Court explained in *Maryland Casualty Co.* v. *Pacific Coal & Oil Co.*, 312

U.S. 270, 273 (1941), "[b]asically, the question in each case is whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment."

In addition, as the Court noted in *Public Service Commission* v. *Wycoff Co.*, 344 U.S. 237 (1952), "the propriety of declaratory relief in a particular case will depend upon a circumspect sense of its fitness informed by the teachings and experience concerning the functions and extent of federal judicial power." *Id.* at 243. "The disagreement must not be nebulous or contingent but must have taken on fixed and final shape so that a court can see what legal issues it is deciding, what effect its decision will have on the adversaries, and some useful purpose to be achieved in deciding them." *Id.* at 244.

2. *Wycoff* illustrates the sort of claim that this Court has consistently held does *not* present an "actual controversy." A company that transported motion picture film in Utah sought a declaratory judgment, against the state's public utility commission, that the company's business constituted "interstate commerce." 344 U.S. at 239. The Court held that the company's claim was nonjusticiable, emphasizing the abstract nature of the requested declaration: "The complainant in this case does not request an adjudication that it has a right to do, or to have, anything in particular. It does not ask a judgment that the Commission is without power to enter any specific order or take any concrete regulatory step." *Id.* at 244. Rather, the Court explained, the company sought only "to establish that, as presently conducted, [its] carriage of goods between points within as well as without Utah is all interstate commerce. One naturally

asks, so what?" *Ibid.* There was no evidence of "any past, present, or threatened action by the Utah Commission" that would affect the company's business. *Id.* at 240-241. "If there is any risk of suffering penalty, liability or prosecution, which a declaration would avoid, it is not pointed out to us." *Id.* at 245.

Similarly, in *United Public Workers* v. *Mitchell*, 330 U.S. 75 (1947), the plaintiffs sought a declaratory judgment that certain provisions of the Hatch Act were unconstitutional. *Id.* at 82-83. The Court held that the plaintiffs' general assertion of a desire to engage in prohibited political activity did not create a justiciable controversy. *Id.* at 86-91. "We can only speculate as to the kinds of political activity the [plaintiffs] desire to engage in or as to the contents of their proposed public statements or the circumstances of their publication." *Id.* at 90. Absent a more concrete dispute, "[s]uch generality of objection is really an attack on the political expediency of the Hatch Act, not the presentation of legal issues," *id.* at 89, and thus beyond the competence of the federal courts to adjudicate. See, *e.g.*, *Textron Lycoming Reciprocating Engine Div.* v. *United Auto. Workers*, 523 U.S. 653, 660-661 (1998) (no "actual controversy" over voidability of collective bargaining agreement where there was no evidence that either the union or the employer "cared about" voidability); *Golden* v. *Zwickler*, 394 U.S. 103, 109 (1969) (no "actual controversy" in declaratory challenge to state law prohibiting anonymous handbilling in elections because the Congressman targeted by plaintiff's handbills had left Congress and was unlikely to again be a candidate).

By contrast, when the parties are truly adversarial, the dispute is concrete in both its factual and legal dimensions, and the requested declaration will definitively

settle the controversy, the Court has consistently held that relief is appropriate under the Declaratory Judgment Act. In *Maryland Casualty*, for example, an insurance company sought a declaratory judgment that it was not required either to defend litigation brought against the insured by the victim of an automobile accident, or to indemnify the insured if the victim prevailed. The insurance company named both the insured and the victim as defendants. The victim moved to dismiss on the ground that no "actual controversy" existed between himself and the insurance company, and the lower courts agreed. 312 U.S. at 271-272.

This Court reversed, observing that *if* the victim prevailed in his suit against the insured and the insured did not satisfy the resulting judgment, the victim would be entitled to proceed against the insurance company by supplementary process. *Maryland Cas.*, 312 U.S. at 273. That contingent possibility, the Court explained, established an "actual controversy" sufficient to warrant declaratory relief, especially given the potential, if the victim were not a party to the federal action, for conflicting judgments in state and federal court regarding the insurance company's obligations under the policy. *Id.* at 273-274. See, *e.g.*, *Steffel*, 415 U.S. at 459; *Lake Carriers' Ass'n* v. *MacMullan*, 406 U.S. 498, 506-508 (1972); *Public Utilities Comm'n* v. *United States*, 355 U.S. 534, 538-539 (1958); *Altvater*, 319 U.S. at 363-365; *Aetna Life*, 300 U.S. at 242-244.

### B. The Court Of Appeals Has Erected An Unwarranted Obstacle To Declaratory Relief In Patent Cases

Despite this Court's more nuanced approach, the Federal Circuit has adopted an inflexible two-step test for declaratory relief in patent litigation. Pet. App. 7a-

8a. Under that test, "[t]here must be both (1) an explicit threat or other action by the patentee, which creates a reasonable apprehension on the part of the declaratory judgment plaintiff that it will face an infringement suit, and (2) present activity which could constitute infringement or concrete steps taken with the intent to conduct such activity." *Gen-Probe*, 359 F.3d at 1380 (quoting *BP Chems. Ltd.* v. *Union Carbide Corp.*, 4 F.3d 975, 978 (Fed. Cir. 1993)); see Pet. App. 7a-8a. As the "reasonable apprehension" prong has been applied in the licensor-licensee context, moreover, the risk of litigation must be more than contingent (*e.g.*, contingent on the refusal to make the payments under the license)—the declaratory judgment plaintiff must face an actual, present apprehension of suit for an injunction, damages, or other coercive relief. See, *e.g.*, *id.* at 5a-6a. In other words, the declaratory judgment plaintiff must already have taken steps that expose it to a risk of suit.[8]

Proof that the declaratory judgment plaintiff labored under a reasonable anticipation of suit is certainly a valid means of establishing that an "actual controversy" exists. But the Federal Circuit effectively treats its two-step test as an all-encompassing restatement of the "actual controversy" requirement in the patent context, and essentially requires a breach before allowing a licensee to sue. See, *e.g.*, Pet. App. 7a-8a; *Gen-Probe*, 359 F.3d at 1379-1380. As a result, the Federal Circuit's test artificially and impermissibly limits the broad power of the federal courts to hear and decide concrete disputes be-

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[8] In at least one recent case, moreover, the court of appeals added the further gloss that an infringement suit by the patentee must be "imminent." See *Teva Pharm. USA, Inc.* v. *Pfizer, Inc.*, 395 F.3d 1324, 1334 (Fed. Cir. 2004), cert. denied, 126 S. Ct. 473 (2005).

tween adverse parties in appropriate declaratory judgment actions.

1. This Court has never suggested that a declaratory judgment plaintiff must face a present risk of suit for coercive relief before an Article III case or controversy will exist. To the contrary, the Court has specifically refused to equate "actual controversy" with the existence of an accrued cause of action for a coercive remedy. In the context of pre-enforcement challenges to criminal statutes, for example, Article III requires a declaratory judgment plaintiff to demonstrate that he faces a "genuine threat of enforcement" if he violates the proscription in question, *Steffel*, 415 U.S. at 475, and that he would be reasonably likely to engage in the proscribed conduct without the threat of enforcement, *id.* at 459. If that showing is made, however, the Constitution does not further require the plaintiff to "expose himself to actual arrest or prosecution" before a declaratory judgment will issue. *Ibid.*; see *Babbitt* v. *United Farm Workers Nat'l Union*, 442 U.S. 289, 301-302 (1979) (allowing plaintiffs to bring challenge to statutory prohibition on false or deceptive speech about agricultural products without a showing that plaintiffs had already violated the prohibition). Indeed, forcing the putative declaratory judgment plaintiff to take the step that actually exposes him to liability would frustrate the purposes of the Declaratory Judgment Act. See pp. 18-19, *infra*. Yet the court below, applying its "reasonable apprehension" test, essentially obligates patent licensees to take such a step in order to create a justiciable controversy, requiring the licensee to "materially breach[] its license," *Gen-Probe*, 359 F.3d at 1382, and thereby subject itself to the risk of an injunction and an award of

damages (potentially including treble damages and attorneys fees). See 35 U.S.C. 283, 284, 285.

There is no justification for imposing a heightened standard for justiciability in the patent context. In fact, this Court has expressly rejected the argument that a licensee's ongoing payment of patent royalties negates any justiciable dispute over the validity of the patent. In *Altvater*, *supra*, the patentees brought suit against two of their licensees to compel specific performance of the territorial restrictions in their license agreement. The licensees filed a counterclaim seeking, *inter alia*, a declaratory judgment that the underlying patents were invalid. 319 U.S. at 360-361. The licensees continued to pay royalties to the patentees "under protest," however, based both on the license agreement itself and on an injunction that the patentees had obtained in earlier litigation against the same licensees. *Id.* at 361-362. As in this case, the licensees explicitly sought to retain the right to perform under the license agreement in the event the patents were held valid and the agreement binding. See *id.* at 361. And as in this case, the patentees opposed the declaratory judgment on the ground that "so long as [the licensees] continue to pay royalties, there is only an academic, not a real controversy, between the parties." *Id.* at 364.

The Court rejected that argument and held the declaratory judgment claim justiciable, explaining that "[t]he fact that royalties were being paid did not make this a 'difference or dispute of a hypothetical or abstract character.'" *Altvater*, 319 U.S. at 364 (citation omitted). Rather, "[a] controversy was raging," and "[t]hat controversy was 'definite and concrete, touching the legal relations of parties having adverse legal interests.'" *Ibid.* To be sure, "[r]oyalties were being demanded and

royalties were being paid. But they were being paid under protest and under the compulsion of an injunction decree." *Id.* at 365. Indeed, "[i]t was to lift the heavy hand of that tribute from the business that the counterclaim was filed. Unless the injunction decree were modified, the only other course was to defy it, and to risk not only actual but treble damages in infringement suits." *Ibid.* (footnote omitted).

The court of appeals in *Gen-Probe* attempted to distinguish *Altvater* on the ground that the licensees' ongoing royalty payments in *Alvater* were not merely required by contract, but compelled by injunction. See 359 F.3d at 1381-1382. From the perspectives of Article III and the Federal Circuit's own test, there is no significance to that distinction. The licensees in *Altvater* would have failed the Federal Circuit's "reasonable apprehension of suit" test just as petitioner did. Yet the Court had little difficulty concluding that there was an "actual controversy" between the parties. That "actual controversy" flowed not from the injunction but from the dispute between the parties, "the heavy hand of * * * tribute," and the prospect of treble damages from infringement, all of which are present here.[9]

2. The court of appeals' test is inconsistent with the fundamental purposes of the Declaratory Judgment Act. It is clear that Congress did not intend the "actual controversy" requirement to obligate the declaratory judgment plaintiff to expose itself to a suit for coercive relief.

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[9] Nothing in *Altvater* indicates that the injunctive nature of the licensees' royalty obligation was dispositive. To the contrary, the Court expressly contemplated that the licensees had the option of ceasing payments and thereby risking "not only actual but treble damages in infringement suits." 319 U.S. at 365. Petitioner's options here are not meaningfully different.

To the contrary, one of the oft-stated purposes of the Declaratory Judgment Act was to enable parties to obtain a declaration of their rights in a dispute without needlessly exposing themselves to an injunction or liability for damages.

Congress recognized that, under the pre-Act state of affairs, it was "often necessary to break a contract or a lease, or act upon one's own interpretation of his rights when disputed, in order to present to the court a justifiable controversy." S. Rep. No. 1005, *supra*, at 3. The Act addressed that dilemma by "enabl[ing] disputes arising out of written instruments, or otherwise, to be adjudicated without requiring a destruction of the status quo." *Id.* at 6; see H.R. Rep. No. 1264, 73d Cong., 2d Sess. 2 (1934) ("If the meaning of a contract is controverted, for example, it may be needless to break it in order to obtain authoritative construction of the instrument, thus saving time and cost."); see also *Steffel*, 415 U.S. at 466-468 (observing that an express purpose of the Declaratory Judgment Act was to permit pre-enforcement challenges to unconstitutional state criminal statutes). The court of appeals' view that a party to a licensing agreement must breach the agreement before maintaining a declaratory judgment action in the patent context is simply irreconcilable with Congress's purposes in adopting the Act.

### C. Petitioner's Declaratory Challenge To The Cabilly II Patent Presents An "Actual Controversy"

Petitioner's challenge to the validity of the Cabilly II patent and its claim of non-infringement comprise "a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to

warrant the issuance of a declaratory judgment." *Maryland Cas.*, 312 U.S. at 273.

1. In this case, the parties' interests are adversarial, the factual and legal dimensions of their dispute are clear, and a declaratory judgment would conclusively resolve the issues that divide them. Petitioner is making royalty payments to respondents under a patent that petitioner claims is either invalid or not infringed by its Synagis® product (or both). Pet. App. 4a, 28a-29a. Respondents insist that the Cabilly II patent covers petitioner's sales of Synagis® and that, under the terms of the licensing agreement, petitioner must pay them royalties. *Id.* at 4a; J.A. 419-420. Although petitioner agreed, under implicit threat of suit (*ibid.*), to pay royalties after the issuance of the Cabilly II patent, it did so with the explicit warning that its payments were made "under protest and with reservation of all of our rights." J.A. 426; see J.A. 133. Furthermore, respondents do not dispute that, if petitioner had not begun paying royalties, it likely would have brought suit for infringement, breach of contract, or both.

Those facts amply demonstrate the existence of a concrete "case or controversy" under the standards enunciated by this Court for purposes of Article III and the Declaratory Judgment Act. Petitioner's contention that the Cabilly II patent is invalid and not infringed by Synagis® is wholly unlike the abstract complaints that this Court held unfit for judicial resolution in *Wycoff*, *Mitchell*, and similar cases. Indeed, respondents have not identified any respect in which this case is actually unfit for resolution by declaratory judgment, apart from the fact that there is a license agreement between the parties covering the Cabilly II patent.

2. There is no basis for concluding that the existence of a license agreement somehow transforms what would otherwise be an "actual controversy" into a non-justiciable request for an advisory opinion. For purposes of Article III and the Declaratory Judgment Act, it is simply immaterial that petitioner has entered a license agreement in order, *inter alia*, to avoid potential liability for infringement and has not breached its license agreement with respondents. What matters instead is whether there is a genuine dispute between the parties that is sufficiently concrete, specific, and substantial to warrant judicial intervention. *Maryland Cas.*, 312 U.S. at 273. If that standard is satisfied, as it is here, the fact that the parties previously agreed to enter into a licensing arrangement does not negate the existence of a controversy "of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *Ibid.* Indeed, when a licensing agreement involves royalty payments from a licensee that disputes the validity of the patent, the agreement is better understood as evidence of (not an obstacle to) a concrete controversy.[10]

The Federal Circuit's contrary rule, if applied consistently, would produce still further incongruous results. The requirement of a "reasonable apprehension of suit" would generally prevent non-breaching licensees from

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[10] Even if one views a license as an agreement by the *patentee* not to sue for infringement, see Pet. App. 7a; *De Forest Radio Tel. Co.* v. *United States*, 273 U.S. 236, 242 (1927), the license agreement is not a concession by the *licensee* of the validity or applicability of the patent, much less an agreement not to sue. *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969). The licensee has entered into the agreement against the inherently coercive backdrop of the presumption of validity and the powerful remedies afforded by the law to the patentee. See *Altvater*, 319 U.S. at 365.

seeking court action to resolve even those contractual disputes beyond validity and infringement. For instance, if petitioner had claimed that the license only obligated it to pay royalties at rate *A*, and respondents believed the license in fact obligated petitioner to pay royalties at higher rate *B*, that would seem to be a paradigmatic scenario for use of the declaratory judgment remedy. But, under the Federal Circuit's "reasonable apprehension of suit" test, as long as petitioner was paying respondents the higher rate *B*, even if under protest, it apparently could not bring a declaratory judgment action to settle that very real dispute.

The Federal Circuit's requirement of an open breach is antithetical to the purposes of the Declaratory Judgment Act and has no basis in any constitutional or statutory limitation on the power of federal courts. This Court's conclusion in *Altvater* applies with equal force here: Petitioner continues to pay royalties, but seeks a declaratory judgment to "lift the heavy hand of that tribute" from its business. 319 U.S. at 365. Like the licensees in *Altvater*, petitioner's only other choice is to breach the license agreement and "risk not only actual but treble damages in [an] infringement suit[ ]," *ibid.*, together with an injunction against the sale of a product that accounts for over 80% of its revenues. And because there is little doubt, based on respondents' immediate demand for royalties after the issuance of the Cabilly II patent, that petitioner faced a genuine risk of suit if it ceased paying royalties, all of the requirements of Article III justiciability are met. "It was the function of the

Declaratory Judgment Act to afford relief against such peril and insecurity." *Ibid.*[11]

### D. The Judgment Below Cannot Be Justified By Considerations Of Patent Policy

The Federal Circuit found support for its strict interpretation of the "actual controversy" requirement in the policies of the federal patent laws. Pet. App. 7a; see *Gen-Probe*, 359 F.3d at 1382. The court stressed the "inequity" it believed would result from a rule that allowed a licensee to challenge the patent under which it is licensed, while "the patent owner, having contracted away its right to sue, is in continuing risk of attack on the patent whenever the licensee chooses—for example, if the product achieves commercial success." Pet. App. 7a. Such inequity must be avoided, the court of appeals stated in *Gen-Probe*, because it would needlessly "discourage patentees from granting licenses." 359 F.3d at 1382.

Considerations of patent policy, however, could not justify creation of a patent-specific test that is more rigorous than the constitutional and statutory standards that determine the existence of a justiciable case or controversy in all other contexts. And in any event, the applicable policy considerations (to the extent they are relevant at all) point in the opposite direction. While patent licensing in general should be encouraged be-

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[11] When the licensor is the United States, however, declaratory remedies may nevertheless be unavailable for other jurisdictional reasons. For example, although a variety of federal agencies license patented technologies to the private sector, claims by licensees against the United States under such agreements would generally have to be brought pursuant to the Tucker Act, which normally does not authorize declaratory relief. See 28 U.S.C. 1491; *United States v. Mitchell*, 463 U.S. 206, 216 n.15 (1983).

cause it allows the efficient exploitation of technology and promotes competition and innovation, see *DOJ/FTC Licensing Guidelines* 4-6, public policy strongly favors ridding the economy of invalid patents, which impede efficient licensing, hinder competition, and undermine incentives for innovation.

1. As an initial matter, the standards governing the "actual controversy" inquiry do not vary depending on a court's assessment of the policy considerations at issue. This Court has made clear that those standards are derived from Article III itself, and that the Declaratory Judgment Act is operative "in respect to controversies which are such in the constitutional sense." *Aetna*, 300 U.S. at 240. Considerations of patent policy cannot change the constitutional analysis, and so the court of appeals' conclusion logically precludes Congress from responding based on its own assessment of patent policy. By declaring that "the *jurisdictional requirements* of a declaratory action *are not met* when royalties are fully paid to the licensor and there is no ground on which the licensor can cancel the license or sue for infringement," Pet. App. 6a (emphasis added), the court of appeals effectively placed the problem beyond the power of Congress to redress. If the court's judgment were properly grounded in Article III that consequence would be unavoidable. But Article III poses no obstacle to suits like this, and considerations of patent policy are properly evaluated by Congress, not by the courts in construing the Act's "actual controversy" requirement, which applies equally to all manner of disputes.

2. In any event, the Federal Circuit also erred in its assessment of the applicable policy considerations. The court's desire to protect patentees from the burden of defending their patents against litigation challenges

cannot be reconciled with *Altvater* (see pp. 17-18, *supra*) or *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969). To be sure, as the court of appeals recognized, *Lear* involved the substantive doctrine of "licensee estoppel," not the "actual controversy" requirement of the Declaratory Judgment Act. Pet. App. 5a-6a. But *Lear*'s holding is based on the strong federal policy favoring "full and free competition in the use of ideas which are in reality a part of the public domain," 395 U.S. at 670, a point that this Court has repeatedly underscored. See, *e.g.*, *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83, 100-101 (1993) (noting the "importance to the public at large of resolving questions of patent validity"); *Blonder-Tongue Labs., Inc.* v. *University of Ill. Found.*, 402 U.S. 313, 349-350 (1971) (describing the Court's "consistent view" that "the holder of a patent should not be insulated from the assertion of defenses and thus allowed to exact royalties for the use of an idea that is not in fact patentable or that is beyond the scope of the patent monopoly granted"); *Edward Katzinger Co.* v. *Chicago Metallic Mfg. Co.*, 329 U.S. 394, 400 (1947) (noting the "necessity of protecting our competitive economy by keeping open the way for interested persons to challenge the validity of patents which might be shown to be invalid").

In light of those precedents, the court of appeals was wrong to suggest that it would be "inequit[able]" to permit licensees who otherwise satisfy the requirements for declaratory relief to challenge the validity of the patents under which they are licensed. Pet. App. 7a. Indeed, the Declaratory Judgment Act reflects a general judgment that it is equitable (and indeed desirable) to allow contracting parties with a dispute regarding their agreement to litigate the dispute without the necessity of an open breach. There is no basis for a special rule for pat-

ent licensees. To the contrary, when a justiciable controversy is present under the general principles of Article III, equitable considerations will normally counsel in favor of permitting such challenges in the patent context, because "[i]t is the public interest which is dominant in the patent system." *Mercoid Corp.* v. *Mid-Continent Inv. Co.*, 320 U.S. 661, 665 (1944). And, as *Lear* observed, "[l]icensees may often be the only individuals with enough economic incentive to challenge the patentability of an inventor's discovery." 395 U.S. at 670.

The Federal Circuit's specific concerns about discouraging the licensing of patents and encouraging gamesmanship by licensees, see Pet. App. 7a; see also *Gen-Probe*, 359 F.3d at 1382, are overstated. Many patents are clearly valid, and thus are unlikely to be challenged. Many patent holders affirmatively desire to license their patents, and many licensees enter licensing agreements with no intent of challenging the validity of the licensed patent. Patent litigation is extremely expensive and lengthy, and often both sides will have an incentive to avoid that expense. See, *e.g.*, *Cardinal Chem.*, 508 U.S. at 99; *FTC Innovation Report*, Exec. Summary 7-8 & n.25 (noting, in 2003, that "[a] biotechnology case, for example, can cost between five and seven million dollars and take two or three years to litigate"). Moreover, there will often be other considerations, such as the existence of cross-licensing arrangements or the desire to preserve valuable business relationships, that will militate against initiation of costly and disruptive patent litigation by licensees. Indeed, the Federal Circuit's concerns are further undercut by the fact that before the creation of the Federal Circuit, case law in a number of circuits supported the notion

that licensees did not have to breach or terminate their license agreements in order to bring a declaratory action.[12]

In any event, to the extent that rejecting the *Gen-Probe* rule does encourage licensees to challenge patents through litigation, that result furthers—rather than hinders—good patent policy. As this Court has recognized, if licensees "are muzzled, the public may continually be required to pay tribute to would-be monopolists without need or justification." *Lear*, 395 U.S. at 670. The Federal Circuit's rule engenders precisely that result, and thus cannot be justified on policy grounds.

3. Application of traditional "case or controversy" principles in the patent context does not leave patent owners defenseless. See *Blonder-Tongue*, 402 U.S. at 335 (noting that "patentees are heavily favored as a class of litigants by the patent statute"). The Patent Office has conferred upon the patentee a valuable property right that is "buttressed by the presumption of validity which attaches to his patent." *Lear*, 395 U.S. at 670; see 35 U.S.C. 282. Indeed, the Federal Circuit has held that "[o]vercoming the presumption requires a showing of facts proved by clear and convincing evidence." *Invitrogen Corp.* v. *Biocrest Mfg., L.P.*, 424 F.3d 1374, 1378 (Fed. Cir. 2005). This Court has thus recognized that it is not "unfair to require a patentee to defend the Patent Office's judgment when his licensee places the question in issue." *Lear*, 395 US. at 670.

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[12] See *Precision Shooting Equip. Co.* v. *Allen*, 646 F.2d 313, 314-319 (7th Cir.), cert. denied, 454 U.S. 964 (1981); *Warner-Jenkinson Co.* v. *Allied Chem. Corp.*, 567 F.2d 184, 187-188 & n.4 (2d Cir. 1977); *American Sterilizer Co.* v. *Sybron Corp.*, 526 F.2d 542, 545-547 (3d Cir. 1975).

In addition, a patent owner may be able to negotiate license provisions that anticipate and ameliorate the effects of the filing of a declaratory judgment action by a licensee. This Court has held that a patentee cannot require a licensee to abandon forever its right to challenge a patent, see *Pope Mfg. Co.* v. *Gormully*, 144 U.S. 224, 232-237 (1892), and that a licensee who successfully challenges a patent cannot be required to pay royalties during the pendency of the challenge, see *Lear*, 395 U.S. at 673-674. But a licensor may be able to make the filing of a declaratory judgment action a basis for terminating the license, changing the royalty rate to a specified higher rate, or otherwise adjusting the pre-challenge terms. Cf., *e.g.*, Restatement (Second) of Contracts § 356(1) (1981) ("Damages for breach by either party may be liquidated in the agreement but only at an amount that is reasonable in light of the anticipated or actual loss caused by the breach and the difficulties of proof of loss."). While the enforceability of such provisions is an open question in light of the strong public policy favoring patent challenges as reflected in *Pope* and *Lear*, those decisions do not necessarily entitle a licensee both to challenge the licensed patent and to retain all the benefits of his license agreement, if the agreement expressly provides otherwise. Cf. *Cordis Corp.* v. *Medtronic, Inc.*, 780 F.2d 991, 995 (1985) (explaining the Federal Circuit's view that *Lear* "*does* permit a licensee to cease payments due under a contract while challenging the validity of a patent. It *does not* permit the licensees to avoid facing the consequences that such an action would bring."), cert. denied, 476 U.S. 1115 (1986). In addition, a would-be licensee that makes clear that it disputes the validity or applicability of the patent may not receive the same terms as other licens-

ees. Patentees concerned about potential litigation could, for example, require prospective licensees to purchase a fully paid-up license. Therefore, the Federal Circuit's assumption that permitting suits like this will necessarily allow licensees to lock in a favorable rate and then sue may be unfounded.

4. For the foregoing reasons, the Federal Circuit's patent-policy concerns cannot justify its conclusion that declaratory actions by licensees in good standing are nonjusticiable under Article III. That is not to say, however, that district courts will be compelled to adjudicate every such dispute. As this Court has made clear, "district courts possess discretion in determining whether and when to entertain an action under the Declaratory Judgment Act, even when the suit otherwise satisfies subject matter jurisdictional prerequisites." *Wilton* v. *Seven Falls Co.*, 515 U.S. 277, 282 (1995). Those considerations apply in patent cases just as they do in all other types of declaratory judgment actions.

Whatever the precise bounds of discretion under the Declaratory Judgment Act, however, see *Wilton*, 515 U.S. at 290, it would be inappropriate for a district court to decline to exercise jurisdiction merely on the ground that the declaratory judgment plaintiff is a licensee in good standing. To do so would be inconsistent with the reasoning of *Lear*, which is founded on the principle that the interests of federal patent law are furthered by allowing licensees to challenge the validity of patents. The *Lear* Court carefully weighed the underlying justifications for the traditional contractual doctrine of licensee estoppel against the "important public interest" in encouraging challenges to potentially invalid patents, and concluded that "the technical requirements of contract doctrine must give way before the demands of the

public interest in the typical situation involving the negotiation of a license after a patent has issued." 395 U.S. at 670-671. That determination forecloses any suggestion that vestigial notions of licensee estoppel can be employed to justify the creation of new obstacles to the adjudication of such challenges.

Beyond that, it is not necessary for the Court to determine under what circumstances a district court might decline to entertain a declaratory action by a licensee. The district court in this case had no occasion to consider that question, because *Gen-Probe* compelled it to dismiss the action. That court is in the best position to address any such discretionary matters in the first instance. See *Wilton*, 515 U.S. at 289 (vesting "district courts with discretion in the first instance, because facts bearing on the usefulness of the declaratory judgment remedy, and the fitness of the case for resolution, are peculiarly within their grasp").

## CONCLUSION

The judgment of the court of appeals should be reversed.

Respectfully submitted.

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# In the Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

v.

GENENTECH, INC., *et al.*,

*Respondents.*

On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

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## INTEREST OF THE *AMICI* [1]

The *Amici* have been leaders in America's technological innovation for over 100 years. Their patent portfolios protect their enormous investments in research and development, and they regularly rank near the top of the annual list of United States patent recipients. They have longstanding and extensive patent licensing experience, both as licensors and licensees. Many of these licenses are entered in settlement of actual or potential patent litigation.

The *Amici* are well acquainted with the various issues that have spurred calls for changes in the patent system. This is not the case to address such issues. No one is contending here that any of the millions of extant patents should be exempted from challenge. But creating a unilateral right for a licensee to challenge a licensed patent ***will not*** address the underlying issues that have triggered efforts for patent reform, ***will*** destabilize thousands of existing patent settlements and license agreements, ***will*** make patent litigation more difficult to settle, and ***will*** have chilling effects on pro-competitive patent licensing and technology transfer activities that generate billions of dollars annually. Changes to the longstanding rules underlying patent settlements and licensing must balance competing policy questions that are best left to Congress, not courts.

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[1] Counsel for a party did not author this brief in whole or in part, and no party other than *Amici* made a contribution toward the preparation and submission of this brief. All parties have consented in writing to the filing of this brief, and their letters of consent have been filed with the Clerk.

*Amicus* 3M Co., which began operations in 1902, is a diversified technology company with a global presence in the health care, industrial, display and graphics, consumer and office, safety, security and protection services, electronics and telecommunications, and transportation markets. 3M sells more than 50,000 goods and services to customers around the world. Annual R&D spending at 3M exceeds $1 billion, and to protect this investment, 3M owns over 7,000 United States patents and over 19,000 patents around the world. In 2005, 3M was awarded 487 United States patents.

*Amicus* General Electric Co. is one of the largest and most diversified industrial corporations in the world. Since its incorporation in 1892, GE has developed a wide variety of products for the generation and utilization of electricity. GE is a major supplier of other technologies and services in fields as varied as healthcare, homeland security, financial services, and entertainment. Total research and development expenditures at GE were $3.4 billion in 2005. GE also has a substantial patent portfolio, with over 18,000 United States patents, 1,180 of which were issued last year.

*Amicus* The Procter & Gamble Company, founded in 1837, is the largest consumer products company in the world. It markets over 300 products, including 22 brands with one billion dollars or more in sales, in 140 countries. Research and product development are central to Procter & Gamble's success as reflected by approximately $1.8 billion in annual R&D spending and over 25,000 patents throughout the world.

*Amicus* E.I. du Pont de Nemours and Company is a science company. Founded in 1802, it is a world leader in science and technology in a range of disciplines, including biotechnology, electronics, materials science safety and security, and synthetic fibers. In 2005, DuPont's research and development expenditures were $1.3 billion and it was granted approximately 400 United States patents. Since 1804, when company founder E.I. du Pont was granted DuPont's first patent, DuPont has been awarded nearly 34,000 U.S. Patents.

## SUMMARY OF THE ARGUMENT

This is not a contract case. Rather, MedImmune seeks a declaratory judgment on a patent, and not on the terms of the corresponding patent license. As a result, MedImmune's central reliance on contract-centered declaratory judgment actions is misplaced. With the focus properly placed on patent declaratory judgment actions, the Federal Circuit's long-standing test is a sensible, patent-specific application of this Court's requirement for an imminent dispute over the subject matter of the case.

MedImmune's proposed new rule would give a licensee a right to bring a declaratory judgment action where the licensor is blocked by the license from bringing the mirror image action for patent infringement, even by way of compulsory counterclaim. Such an asymmetric rule is inconsistent with the language of the Declaratory Judgment Act, will undermine existing settlement and license agreements by giving licensees new rights for which they never paid, and will chill patentees from settling infringement suits and licensing their technology out of concerns that once they bargain away part of their valu-

able patent rights, their licensees will turn around and challenge the licensed patents.

## ARGUMENT

### I. MEDIMMUNE WRONGLY ANALOGIZES TO CONTRACT ACTIONS

This is a declaratory judgment action for patent invalidity, unenforceability, and noninfringement.[2] The mirror image action is for patent infringement. This is not an action to clarify the terms of, or rights under, MedImmune's patent license. As a result, the focus must be on whether there is an imminent risk of patent infringement litigation here. Because Respondents are blocked by the license from bringing a patent suit, there is no such risk and no subject matter jurisdiction.

#### A. Because This Is a Patent Action, Comparisons to Contract Actions Are Inapt

To determine whether jurisdiction exists for a declaratory judgment claim, courts look to the "mirror image" action that the declaratory judgment defendant would normally have brought. *See, e.g., Skelly Oil Co. v. Phillips Petroleum Co.*, 339 U.S. 667, 673-74 (1950) (holding that subject matter jurisdiction for a declaratory judgment action is lacking where "artful pleading anticipates a defense based on federal law"); *see also Franchise Tax Bd. v. Constr. Laborers Vacation Trust*, 463 U.S. 1, 16

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[2] Count 1 of MedImmune's Complaint does refer to the license, but MedImmune does not rely on that Count on appeal, perhaps because the parties are not diverse, so that jurisdiction must be supported by the patent claim in any event.

(1983) ("*Skelly Oil* has come to stand for the proposition that 'if, but for the availability of the declaratory judgment procedure, the federal claim would arise only as a defense to a state created action, jurisdiction is lacking.'"). Here, the mirror image action is one for patent infringement, because MedImmune seeks a declaration of patent invalidity, unenforceability, and noninfringement [Pet. Br. at 7-8], and not an action under its patent license. *See, e.g., Rivet v. Regions Bank of La.*, 522 U.S. 470, 475 (1998); *Public Serv. Comm'n of Utah v. Wycoff Co.*, 344 U.S. 237, 248 (1952) ("[I]t is the character of the threatened action, and not of the defense, which will determine whether there is federal-question jurisdiction.").

MedImmune and its *amici*, including the government, overlook the fundamental distinction between this case and actions that seek a declaration of rights under a contract.[3] In a declaratory judgment suit brought under a contract, either party can sue when a real dispute exists over the meaning of terms in the contract. In contrast, MedImmune seeks a right to enter into a license, and thereby obtain the protection from a patent infringement suit the license provides, while retaining a unilateral right to challenge the patent whenever it desires. This one-

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[3] One *amicus* brief highlights the misinterpretation of this case as a contract action rather than a patent action in the following heading: "The Federal Circuit Decisions Fail to Follow the Well-Established Principle that a Case and Controversy Sufficient to Sustain Jurisdiction Exists When the Parties to a Contract ***Have a Bona Fide Dispute Over Its Proper Interpretation.***" [Medtronic Br., at 8 (emphasis added)].

sided rule is wholly dissimilar to the symmetrical rights that both parties to a contract have to bring suit in order to ensure that its terms are being followed.

With the focus properly set on patent infringement actions, the Federal Circuit's two-part test for declaratory judgment subject matter jurisdiction is entirely appropriate for identifying those cases that present a "definite and concrete controversy" of "sufficient immediacy and reality."[4] The Federal Circuit's test requires, first, that the ***patentee*** has acted in a manner that would give the declaratory judgment plaintiff a reasonable apprehension that the patentee will sue if the allegedly infringing activity continues. This prong ensures that there is a real and definite controversy, and not simply a unilateral fear by the declaratory judgment plaintiff. *See Fina Oil & Chem. Co. v. Ewen*, 123 F.3d 1466, 1470 (Fed. Cir. 1997). The second prong requires a showing that the declaratory judgment plaintiff has produced, or prepared to produce, the accused item. This prong ensures that the dispute is sufficiently immediate. *See id.* In sum, the Federal Circuit's two-part test accords perfectly with the general requirement that there must be a definite and immediate dispute between the parties.

The Federal Circuit has not, however, limited declaratory judgment jurisdiction to the two-part test. Rather, it has supplied the test as one exemplary way to establish the presence of a case or contro-

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[4] *See Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240 (1937); *Md. Cas. Co. v. Pacific Coal & Oil Co.*, 312 U.S. 270, 273 (1941).

versy, but has consistently left open for declaratory judgment plaintiffs to establish a case or controversy in other ways. *See, e.g., id* ("Satisfaction of this traditional two-part test is not, however, a prerequisite to jurisdiction in every possible patent declaratory judgment action."); *Arrowhead Indus. Water, Inc. v. Ecolochem, Inc.*, 846 F.2d 731, 735-36 (Fed. Cir. 1988) (acknowledging the statement in *Md. Cas. Co.*, 312 U.S. at 273, that "it would be difficult, if it would be possible, to fashion a precise test for determining in every case whether there is such a controversy," to note that "[a] test ***often useful*** in evaluating complaints for declaratory judgments in patent cases" is the two-part test) (emphasis added).

Thus, while the Federal Circuit recognizes the need for flexibility, it has properly acted to give parties a guide for evaluating whether a justiciable case or controversy exists in the most common fact pattern arising in the patent context. But there simply can be no justiciable controversy absent some real and immediate act of provocation ***by the patentee***.[5]

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[5] The government's brief argues that an actual controversy exists because "[a]bsent respondents' patent, and their claim that petitioner's principal product infringes that patent, petitioner would not be paying royalties to respondents on its sales of that that product." [Brief of United States, at 10]. This one-sided argument from the licensee's perspective ignores this Court's precedent requiring a real and immediate dispute, as shown by the threat of litigation of the mirror image action, as a prerequisite for declaratory judgment subject matter jurisdiction. It likewise abandons the concept of symmetry and would eviscerate the bargain reached by the parties and embodied in the license agreement, which re-

Indeed, there are millions of patents currently extant in the U.S., and the owners of those patents cannot be hauled into court if they have not taken some action to threaten another party with suit. This Court has rejected claims by declaratory plaintiffs where no threatening action has occurred against those plaintiffs. *See, e.g., id.*; *Babbitt v. United Farm Workers Nat'l Union*, 442 U.S. 289, 298 (1979) (noting that a plaintiff that fails to claim even a threat of prosecution cannot invoke the federal courts' jurisdiction); *see also City of Los Angeles v. Lyons*, 461 U.S. 95, 101-02 (1983) (plaintiff must show threat of injury that is "real and immediate."). Patent owners that have agreed to share their technology through licensing should not be disadvantaged, in essence waiving any challenge to declaratory judgment subject matter jurisdiction each time they license a patent.

### B. Subject Matter Jurisdiction Cannot Arise Solely From a Party's Dissatisfaction Over the Economic Terms of a Patent License Agreement

Even in declaratory judgment actions involving the terms of a contract, this Court has repeatedly required a real and immediate dispute, with a threat of imminent litigation, before jurisdiction will arise. *See, e.g., Textron Lycoming Reciprocating Engine Div., Avco Corp. v. United Automobile, Aerospace and Agric. Implement Workers of Am.*, 523 U.S. 653, 661 (1998) (no jurisdiction over union's effort to void con-

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moves any "actual controversy" that could give rise to the mirror image action for infringement by the licensee.

tract where union never threatened to strike, and the company had no interest in defending the contract). Indeed, none of the cases MedImmune cites found a case or controversy based solely on a contracting party's desire to avoid the contract's economic impact. Rather, in each case there was either a very real and imminent threat of litigation, or special facts that showed the presence of a true controversy. *See Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 95-96 (1993) (live dispute between the parties was shown by the patentee suing the defendant); *Altvater v. Freeman*, 319 U.S. 359, 364-65 (1943) (noting that "[a] controversy was raging, even apart from the continued existence of the license agreement"); *Aetna Life Ins. Co.*, 300 U.S. at 242 (suit against insured who had stopped paying premiums). To confer subject matter jurisdiction, there must be something more than the licensee's dissatisfaction with the terms of the license into which it voluntarily entered

The need for something more than a contractor's wish to get out of a contract is particularly important in the patent license context. Patentees give up substantial rights in entering into a license agreement—moving from a right to sue and obtain powerful remedies, to a right only for royalties. The patentee's voluntary agreement to "stand down" is a clear act by the patentee that wholly eliminates any actual controversy and any subject matter jurisdiction while the patent license remains in place.

## II. CREATION OF A UNILATERAL RIGHT OF LICENSEES TO CHALLENGE A PATENT WHEN THE PATENTEE CANNOT ASSERT THE PATENT WILL MAKE SETTLEMENT OF PATENT LITIGATION MORE DIFFICULT AND WILL UNDERMINE PATENT LICENSING

MedImmune and its *amici* ask this Court to create a wholly asymmetrical rule, by which licensees could file suit unilaterally even though they have induced patentees to give up their right to sue for infringement. This new rule is contrary to established precedent upon which patent licenses have long been structured. It will make patent infringement litigation more difficult to settle, will destabilize existing patent licenses, and will have a chilling effect on virtually every technology transfer via patent licensing in the future.

### A. MedImmune's Proposed New Rule Lacks Necessary Symmetry

The Constitution and the Declaratory Judgment Act provide federal courts with subject matter jurisdiction when there is a "case or controversy" or a "case of actual controversy," respectively. *See* U.S. Const. art. III, § 2; 28 U.S.C. § 2201. These provisions are wholly indifferent to the party bringing suit, and instead focus on the presence or absence of a real controversy. *See Aetna*, 300 U.S. at 244 ("It is the nature of the controversy, not the method of its presentation or the particular party that presents it, that is determinative."); *see also Maryland Casualty Co.*, 312 U.S. at 273 ("It is immaterial that fre-

quently, in the declaratory judgment suit, the positions of the parties in the conventional suit are reversed; the inquiry is the same in either case."). Federal Rule of Civil Procedure 13(a) reflects this basic symmetry by making infringement a compulsory counterclaim to a declaratory judgment action of noninfringement or invalidity. *See Vivid Technologies, Inc. v. Am. Science & Eng'g, Inc.*, 200 F.3d 795, 801 (Fed. Cir. 1999) (collecting cases); *Polymer Indus. Prods. Co. v. Bridgestone/Firestone, Inc.*, 347 F.3d 935, 938-39 (Fed. Cir. 2003) (*citing S. Constr. Co. v. Pickard*, 371 U.S. 57, 60 (1962)). In short, either a case or controversy exists or it does not, irrespective of which party wishes to file suit.

The Federal Circuit's "reasonable apprehension" requirement ensures symmetry. Specifically, a party may bring a declaratory judgment action under the "reasonable apprehension" test when it faces a real and legitimate danger that the licensor could sue it. Of course, a licensor cannot create such a danger until the licensee has breached or the license is otherwise removed (*e.g.*, if the parties have agreed that certain actions by one of the parties will void the contract). The licensee may not sue until the patentee may sue, and vice-versa—a result fully in accord with the party-independent nature of the Declaratory Judgment Act.

### B. Giving Licensees Unilateral Declaratory Judgment Rights Will Discourage Finality in Settlements And Make Patent Owners Wary Of Reaching Future Settlements

Patent license agreements differ from many other types of contracts in that they often represent

settlement of an actual or potential infringement action. Before the license, a patentee has the right to sue for infringement, which may come with the ability to seek, *inter alia*, an injunction, lost profits, and/or enhanced damages for willful infringement from the accused infringer. *See* 35 U.S.C. §§ 283-285. After the license, the patentee has bargained away its right to sue and seek those remedies, and retains only the right to the negotiated royalty payments. A licensee, on the other hand, receives access to the patented technology. And perhaps most important, the licensee obtains "peace" from patent litigation.

When parties agree to opt out of litigation in this way, courts should discourage continuing disputes and litigation over the very rights that formed the basis of the parties' agreement. Patent litigation is a real strain on the resources of parties and courts. It is enormously expensive and disruptive, and often extremely contentious. Encouraging finality in the license agreements whereby willing parties agree upon mutually-acceptable terms to avoid this process is an important goal and one that this Court can advance by affirming. *See Williams v. First Nat'l Bank*, 216 U.S. 582, 595 (1910) ("Compromises of disputed claims are favored by the courts."); *Aro Corp. v. Allied Witan Co.*, 531 F.2d 1368, 1372 (6th Cir. 1976) ("Settlement is of particular value in patent litigation, the nature of which is often inordinately complex and time consuming.").

MedImmune's proposed rule would disrupt past and future settlements. For the past, the rule would give licensees much more than they bargained for. They would get protection from a suit, with the sole

option to sue whenever they choose, without any risk that they will end up worse off if they lose, because their license rights would continue. Licensees alone would have the right to watch the development of technology, of the market, and of the parties' relationship, and if they decided they no longer like the agreed-upon deal (e.g., if they think they negotiated too high a royalty rate, or if they find new prior art to try to invalidate the patent), they could sue the licensee without facing any risk of a patent infringement suit or counterclaim in return. That is a right for which existing licensees did not negotiate, for which they did not pay, and which they do not deserve.

For the future, MedImmune's new rule will make patent infringement litigation much more difficult to settle. Plaintiffs understandably will be worried about defendants "gaming the system" by agreeing to what appear to be reasonable licensing terms; and then, with the license signed and the litigation gone, turning around and bringing a declaratory judgment action. To mitigate the risk of defendants pursuing this "no lose" strategy, plaintiffs will need to insist upon upfront payments, rather than a running royalty that the plaintiff fears the defendant does not intend to pay. Cases that otherwise could have settled with ongoing royalty payments will continue if defendants are unwilling or unable to pay expected royalties in an advance, lump sum payment.

### C. Giving Licensees Unilateral Rights To Challenge Licensed Patents Unbalances The Consideration Underlying Existing Licenses And May Curb The Granting of Future Licenses

The standard that requires a declaratory patent plaintiff to have a "reasonable apprehension of suit for patent infringement" has been in place since as early as 1966, *see Japan Gas Lighter Ass'n v. Ronson Corp.*, 257 F. Supp. 219, 237 (D.N.J. 1966), and has been unshakable law in the Federal Circuit since the court's founding in the early 1980s. *See, e.g., Vanguard Research, Inc. v. Peat, Inc.*, 304 F.3d 1249, 1254-55 (Fed. Cir. 2002); *Serco Servs. Co. v. Kelley Co.*, 51 F.3d 1037, 1038 (Fed. Cir. 1995); *Jervis B. Webb Co. v. Southern Sys., Inc.*, 742 F.2d 1388, 1398-99 (Fed. Cir. 1984). The rules in this area are clear, consistent, and uniform, have been so for decades, and parties are able to work within and in reliance on those rules to effectuate their mutual intent when entering into license agreements.

MedImmune's proposed new rule incongruously would place patent owners that have engaged in procompetitive licensing of their patent rights and technology in a worse position than non-licensing patentees. The latter may generally choose whether and when to sue for infringement, whereas the former (under MedImmune's rule) will open themselves to suit by any licensee that no longer likes its deal. By taking steps to make its patented technology available to others, by avoiding litigation, and without ever threatening any sort of suit, a licensing patentee will create subject matter jurisdiction for challenges to its patent by any licensee, and will be un-

able to bring suit or a counterclaim itself. That rule simply makes no sense.

Innovative companies like the *Amici* have structured their patent licenses around the Federal Circuit's well-established rules, which are an integral part of those deals and the consideration the parties provide to each other. For example, when licensing a patent for its full term, which may extend years into the future, parties expect that issues may come up regarding the patent's validity and the coverage of future products by the license. To address these and many other issues, parties can and do agree to settle licensing disputes using alternative dispute resolution, so that a licensee can address questions without litigation. Such concessions to the licensee are, of course, met with matching consideration to the licensor.

Such compromises are, naturally, part of the full, negotiated deal between the parties. In the end, each of the untold number of patent license agreements currently in place represents a negotiated, private transaction between a willing licensor and licensee that balances the parties' respective interests and the relative strengths of their positions on the issues of the licensed patent's infringement, validity, and enforceability.

The settled expectations of licensing parties, and the inequity of changing the balance of interests—with no compensation to licensors—strongly caution against upsetting the Federal Circuit's sensible and well-established standard for declaratory judgment jurisdiction in the patent context. *See Quill Corp. v. North Dakota*, 504 U.S. 298, 317 (1992) (refusing to overrule a prior decision in part because it had "en-

gendered substantial reliance" by both the courts and industry such that the decision had "become part of the basic framework of a sizable industry"). If any change is to occur to decades-old rules that underlie billions of dollars in ongoing licensing activity, that change should come from Congress, which can consider the policy effects of such a change on existing licenses and the potential for dampening effects on pro-competitive licensing and technology transfer activities in the future.

### D. Patent Licensees Have Many Options Available to Them; MedImmune's Doomsday Scenario Is Hyperbolic

MedImmune suggests that the Federal Circuit's two-part test puts licensees in peril, for they must throw the protection of a license away in order to have their concerns heard by a court—risking, in MedImmune's words, "financial ruin." [MedImmune Br., at 13, 24, 48]. This argument is overblown and ignores many real and practical options available to licensees short of breaching the license agreement.

For example, it is common for license agreements to include safety valves, such as mechanisms for alternative dispute resolution, to deal with changed circumstances during the term of the license.

Specifically, parties can and do agree on arbitration to decide whether a licensee's new products are covered by the license, and thus subject to royalties. Even without such a mechanism in the license, a licensee that wishes to assert that a new product—designed after the parties signed the license—does not infringe is in the same position as any party that develops a product that might, or might not, infringe

a patent. In particular, the licensee may have a unilateral fear about infringement, but in the absence of threats of litigation from the patentee, that is a classic situation of the type that this Court and others have held does not present a case or controversy. *See, e.g., Textron,* 523 U.S. at 661; *Babbitt,* 442 U.S. at 298.

A licensee that enters a license agreement never has—and should not—also automatically obtain the one-sided right to challenge the licensed patent whenever it chooses to launch a new product. The licensee is free to determine whether or not to pay royalties on its new product by balancing the benefits of the license and the costs. If the licensee chooses not to pay royalties, it faces the risk of an infringement suit by the patent owner, and it can bring a declaratory judgment action if it can satisfy the Federal Circuit's two-part test for subject matter jurisdiction.

The licensee is, in fact, in a better position than would be another party worried about infringing a patent, because the licensee can argue that the appropriate level of damages is a reasonable royalty equal to the royalty it agreed to in the license, *see* 35 U.S.C. § 284. Thus, the licensee may be no worse off if it refuses to pay royalties and loses the resulting infringement suit than it is from continuing to pay royalties under the license.

Moreover, unlike a typical infringer, the licensee always has the option of protecting itself by continuing to pay royalties under the license and foregoing litigation. There simply is no peril. And in any event, arguments about risks faced by licensees that sign license agreements they later regret, but are unwilling to terminate, cannot take the place of the

Constitutionally-mandated "case or controversy" requirement. *See, e.g., Golden v. Zwikler*, 394 U.S. 103, 109-10 (1969) (noting that even an important Constitutional issue "must be presented in the context of a specific live grievance.").

Likewise, the parties can agree to deal with questions about a patent's validity via alternative dispute resolution. Even where the license is silent on such alternatives, a licensee has very real options short of breaching the license and filing a declaratory judgment action. For example, the licensee may be able to challenge the patent's validity in front of the experts at the Patent Office using *ex parte* or *inter partes* reexamination proceedings, the latter of which allow the licensee to submit arguments all the way through appeal to the Federal Circuit. *See* 35 U.S.C. §§ 302, 311.

In short, multiple avenues exist to further the public policy favoring challenges to questionable patents—both via negotiated alternative dispute mechanisms and via Patent Office proceedings—without giving scores of existing licensees unilateral rights to bring declaratory judgment actions for which they never bargained in their license agreements, and for which they never provided consideration.[6]

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[6] One *amicus* brief sets up a false "Hobson's Choice" in arguing that companies must forego validity challenges to individual patents when they license entire portfolios. [Medtronic Br., at 6-7]. Regardless of the number of licensed patents or the number of those patents a licensee wishes to challenge, the licensee faces the same cost-benefit decision, i.e., whether the perceived injustice of paying what it believes are

## CONCLUSION

For the foregoing reasons, the *Amici* support the decision of the Federal Circuit and urge affirmance by this Court.

Respectfully submitted,

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unjustified royalties outweighs the benefits it gets from the license. The perceived difficulty in making that decision is no justification for disregarding the Constitutionally-mandated "case or controversy" requirement. And of course, nothing prevents parties from negotiating, for mutually-agreeable consideration, the right to challenge individual licensed patents without terminating the entire agreement.

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(11)

Supreme Court, U.S.
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No. 05-608

IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

v.

GENENTECH, INC., *et al.*,

*Respondents.*

*ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT*

## BRIEF FOR THE AMERICAN BAR ASSOCIATION AS AMICUS CURIAE SUPPORTING RESPONDENTS

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JULY 26, 2006

BEST AVAILABLE COPY

Amicus will address the following questions:

1. Whether the holding of *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969), is limited to validity challenges by repudiating patent licensees and therefore preserved licensee estoppel in validity challenges by nonrepudiating patent licensees.

2. Whether Article III permits a patent licensee to obtain a judicial determination of the merit of an invalidity counterclaim that the licensee could assert if the licensee (a) repudiated the license agreement, (b) infringed the patent, and (c) were sued for infringement by the licensor.

3. Whether, if licensee estoppel would bar a nonrepudiating patent licensee from suing to invalidate the licensed patent, a federal court should decline jurisdiction over such a suit on equitable and prudential grounds.

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## INTEREST OF AMICUS[1]

The American Bar Association is the voluntary, national membership organization of the legal profession. Its more than 407,000 members, from every State and territory and the District of Columbia, include prosecutors, public defenders, private lawyers, legislators, law professors, law enforcement and corrections personnel, law students, and non-lawyer associates in allied fields. Since its inception in 1878, the ABA has promoted improvement of the administration of justice.

At its June 2006 meeting, the ABA's Board of Governors adopted as policy the Federal Circuit's rule that a nonbreaching patent licensee should not be allowed to challenge the validity of the licensed patent. The Board adopted this policy on the recommendation of the Section of Intellectual Property Law, the world's largest intellectual property organization, whose 19,000 members reflect a broad cross-section of the patent bar.[2]

The ABA submits this brief to advise the Court of equitable and prudential considerations that support the Federal Circuit's rule. The ABA submits that a district court, on the basis of these considerations, should decline jurisdiction over validity challenges by nonbreaching licensees,

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[1] The parties have consented to the filing of this brief. No party authored the brief in whole or in part or contributed monetarily to its preparation or submission.

[2] Neither this brief nor the decision to file it reflects the views of any judicial member of the ABA. The brief was not circulated to any member of the Judicial Division Council before filing, and no member of the Council participated in the adoption or endorsement of the positions taken in the brief.

and that the Court therefore need not decide in this case whether Article III compels that result.

## SUMMARY OF ARGUMENT

The Court granted review to decide whether a challenge by a nonbreaching patent licensee to the validity of the licensed patent meets the case-or-controversy requirement of Article III, as implemented by the Declaratory Judgment Act. The ABA respectfully submits that such a challenge does not meet that requirement, but also that the Court need not decide that constitutional question here. As an equitable and prudential matter, a federal district court should decline jurisdiction over such challenges based on the doctrine of licensee estoppel, whether or not an Article III case-or-controversy exists.

**I.** Although the Court in *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969), broadly rejected the doctrine of licensee estoppel, the facts of the case did not require the Court to do so, and the Court's broad rejection of the doctrine produces unfortunate, if unintended, consequences. The Court's holding was correct on the facts of the case; this case presents an appropriate opportunity to limit the reasoning of the decision. On its facts, *Lear* properly stands for the proposition that a patent licensee may, *upon repudiation of the license*, contest the validity of the licensed patent. As the Federal Circuit's decision suggests, *Lear* should not be read to permit a non-repudiating licensee, like Petitioner, to contest the patent's validity.

**II.** The Federal Circuit's conclusion that this case does not present an Article III case-or-controversy is consistent with *Lear*. First, whether under the doctrine of licensee estoppel, or for the other reasons stated by Respondents, Petitioner is not entitled to challenge the licensed patent. As long as Petitioner complies with the license agreement, it has no judicially cognizable right to assert. Second, Petitioner is not suffering injury. Petitioner was not compelled to enter into the license agreement and is not

compelled to continue to perform under the agreement. Petitioner's only "injury" is its uncertainty about its potential legal exposure if it repudiates the license agreement but continues to practice the licensed invention. That is an everyday question for which businesses seek the advice of attorneys, not Article III courts.

**III.** Considerations of practicality and the wise administration of justice counsel that a district court, as an equitable and prudential matter, should decline jurisdiction in a case like this. A rule allowing a non-repudiating licensee to challenge the licensed patent would be contrary to the aims of the Declaratory Judgment Act, federal patent law and policy, and prudential standing principles. Such a rule would permit the licensee to challenge the patent while simultaneously enjoying its benefits, protected by the license from an infringement action by the licensor and competition by non-licensees. Moreover, such a rule would discourage, not promote, challenges to invalid patents. Licensors would insist that licensees agree in the license not to challenge the patent during the term of the license or while the licensee remains in good standing, or require licensees to make front-loaded, non-refundable royalty payments. At worst, such a rule would undermine the statutory goal of encouraging innovation and invention by discouraging patent licensing.

## ARGUMENT

### I. *LEAR* SUPPORTS THE FEDERAL CIRCUIT'S RULE.

In *Lear, Inc.* v. *Adkins*, 395 U.S. 653 (1969), the Court held that a licensee that had repudiated its licensing agreement was free to contest the validity of the licensor's patent. In doing so, however, the Court rejected, as "inconsistent with the aims of federal patent policy," the doctrine of licensee estoppel itself. *Id.* at 673. But the facts of the case did not require the Court to reject the doctrine.

Accordingly, although Petitioner argues that *Lear* cannot be reconciled with the Federal Circuit's rule in this case, *see* Pet. Br. 36-38, a review of the doctrine of licensee estoppel and a careful understanding of the true holding of *Lear* demonstrate that Petitioner is mistaken.[3]

At common law, the doctrine of licensee estoppel prevented a licensee from simultaneously challenging a patent's validity and practicing the invention under the protection of the license. A licensee who repudiated the licensing agreement, however, was free to defend an action for post-repudiation royalties or infringement on invalidity grounds. Thus, even in the absence of a valid termination of the licensing agreement, a licensee could set up a validity challenge.

### A. *Lear* Correctly Rejected Licensee Estoppel in the Case of a Repudiating Licensee.

*Lear* involved a suit for royalties by licensor Adkins after licensee Lear refused to pay royalties under the terms of the parties' licensing agreement. *See* 395 U.S. at 659. Lear defended based, in part, on the asserted invalidity of Adkins' patent. *Id.* at 660. The California Supreme Court held that, "[u]nder the doctrine of licensee estoppel, Lear [is] prohibited from challenging the validity of Adkins' patent" because, although Lear had stopped paying royalties, he had not "validly terminated" the agreement pursuant to its terms. *Adkins* v. *Lear, Inc.*, 67 Cal. 2d 882,

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[3] The development of the common law doctrine of licensee estoppel, and the doctrine's relation to *Lear*, are reviewed in William C. Rooklidge, *Licensee Validity Challenges and the Obligation to Pay Accrued Royalties: Lear* v. *Adkins Revisited, reprinted in* ROGER M. MILGRIM, MILGRIM ON LICENSING app. 8D.

899 (1967). It was this ruling, and only this ruling, that the Court reviewed and reversed in *Lear*.

Although the Court broadly articulated its holding, appearing to reject the doctrine of licensee estoppel *in toto*, what the Court necessarily rejected in *Lear* was only the version of the doctrine applied by the California Supreme Court on the facts of the case. Accordingly, the true holding of *Lear* does not foreclose application of the doctrine to markedly different facts, including those here.

The doctrine that a patent licensee may not challenge the validity of the licensed patent was established in this country by the middle of the nineteenth century. *See Lear*, 395 U.S. at 662. In *Dale Tile Manufacturing Co.* v. *Hyatt*, 125 U.S. 46 (1888), for example, the Court held federal question jurisdiction was lacking where a licensee, who was sued for royalties under the license agreement, defended by challenging the patent. The Court explained that, in "this action to recover royalties due under the agreement, the defendant, *while continuing to enjoy the privileges of the license*, was estopped to deny the validity of the patent or of any reissue thereof." *Id.* at 54 (citing, *inter alia*, *Kinsman* v. *Parkhurst*, 59 U.S. (18 How.) 289 (1855)) (emphasis added).

The italicized portion of the Court's holding was integral to the doctrine of licensee estoppel that the Court described. The application of the doctrine as described in *Hyatt* depended on the fact that the licensee continued to enjoy the privileges of the license. The doctrine would not prevent a licensee who repudiated the licensing agreement from contesting the validity of the license in a suit by the licensor for future royalties or for infringement. Lower courts elaborated but did not extend the doctrine as described by the Court.

In *Universal Rim Co.* v. *Scott*, 21 F.2d 346 (D.N.D. Ohio 1922), for example, the district court considered whether, absent a provision permitting the license agree-

ment to be terminated, a licensee could contest the validity of patents covered by the agreement after renunciation and notice. *Id.* The court answered yes, stating that "the licensee, whenever he ascertains that the patents covered by the license agreement are invalid, may refuse to be further bound thereby, and, upon repudiation and notice, may thereafter defend against an action for royalties or an infringement suit as freely as may a stranger." *Id.* at 348-49.

The district court's holding reflected the "weight of authority" pre-*Lear* – "that the licensee may dispute the validity of the patent under which he is licensed after he has repudiated the license." *Crew* v. *Flanagan*, 242 Minn. 549, 558 (1954) (collecting cases).[4] Because the licensee in *Lear*

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[4] *Accord Martin* v. *New Trinidad Lake Asphalt Co.*, 255 F. 93, 94 (D.N.J. 1919) ("A licensee * * * may not set up the supposed invalidity of the patent * * * unless, prior to the period for which the royalties are sought to be recovered, he has given to the licensor a distinct, definite, and unequivocal notice to the effect that he no longer recognizes the binding force of the agreement.") (collecting cases); *Mudgett* v. *Thomas*, 55 F. 645, 649 (C.C. S.D. Ohio 1893) ("[D]efenses involving the validity of the patent will be available only for the period subsequent to the abandonment of the license by the defendants, and notice thereof to the plaintiffs."); *Marston* v. *Swett*, 82 N.Y. 526, 533 (1880) ("Where the patent is apparently valid and in force the party using it, receiving the benefit of its supposed validity, is liable for royalties agreed to be paid and cannot set up as a defense the actual invalidity of the patent. * * * If the manufacturer does not so intend, and chooses to make the patented article, not under the patent but in hostility to it, he must give notice of that intention, in order that the presumption may not attach or the patentee be misled.").

had repudiated the licensing agreement, the Court had no need to address the issue presented here.

### B. *Lear* Needlessly Rejected Licensee Estoppel in the Case of a Nonrepudiating Licensee.

The Court decided *Lear* on the premise that, under the doctrine of licensee estoppel, a patent licensee could avoid estoppel only by terminating the agreement pursuant to its terms, and that committing a material breach, or otherwise repudiating the agreement, did not suffice. The Court therefore reasoned that, to allow licensees to avoid estoppel, it had to abolish the estoppel doctrine *in toto*. *Lear*, 395 U.S. at 663 n.10.

The Court's premise, however, appears to have been mistaken. The justification for licensee estoppel at common law was that "it would be unreasonable for a licensee to have the advantage of the patent in his commercial dealings with the world at large and repudiate it in his dealings with his licensor when it comes to paying royalties. He must take a stand which is consistent *for he cannot be allowed to affirm and disaffirm the patent at one and the same time.*" *Crew* v. *Flanagan*, 242 Minn. at 558 (emphasis added). *Accord Marston* v. *Swett*, 82 N.Y. at 533 ("The reasons for the rule are that the party has got what he bargained for; that he cannot be allowed at the same time to affirm and disaffirm the patent."). Thus, allowing a licensee to set up an invalidity defense upon repudiation of a licensing agreement would not, as the Court evidently supposed, undermine the vitality of the estoppel doctrine. *See Lear*, 395 U.S. at 663 n.10.

Because the facts of *Lear* did not require the Court to reject licensee estoppel, the Court's rejection of the doctrine is not binding authority. *See Kastigar* v. *United States*, 406 U.S. 441, 454-55 (1972) ("broad language * * * unnecessary to the Court's decision * * * cannot be considered binding authority"); *Cohens* v. *Virginia*, 19 U.S. (6

Wheat.) 264, 399-400 (1821) ("It is a maxim not to be disregarded, that general expressions, in every opinion, are to be taken in connection with the case in which those expressions are used. If they go beyond the case, they may be respected, but ought not to control the judgment in a subsequent suit when the very point is presented for decision.").

### 1. The cases cited by *Lear* do not undermine licensee estoppel.

The Court in *Lear* stated that *St. Paul Plow Works* v. *Starling*, 140 U.S. 184 (1891), undermined the common law doctrine of licensee estoppel. *See Lear*, 395 U.S. at 663. In *St. Paul*, however, the licensee had "renounce[d] its license" long before asserting the patents' invalidity. 140 U.S. at 186. For this reason, the lower court admitted invalidity evidence. Had it succeeded in proving invalidity, the licensee would have been relieved of the obligation to pay post-repudiation royalties. Thus, although inconsistent with the "strong-form" version of licensee estoppel that the Court necessarily rejected in *Lear*, *St. Paul* was consistent with the common law rule of licensee estoppel and the Federal Circuit's rule in this case.

In *Pope Manufacturing Co.* v. *Gormully*, 144 U.S. 224 (1892), the Court was troubled primarily by the fact that the licensing agreement purported to bind the licensee even in the event that the licensor's patent was eventually declared invalid. However, as the *Universal Rim* court explained, "[a] licensee, if evicted from the use of the patents by a judgment of a court of competent jurisdiction declaring the patents invalid, may, after giving notice to the licensor, defend against the payment of royalties subsequently accruing." 21 F.2d at 348. Under the common law rule of licensee estoppel, such "eviction" ended the estoppel. In short, the licensing agreement's infirmities in *Pope* were unrelated to any legitimate application of the licensee estoppel doctrine.

Nor did *Scott Paper Co.* v. *Marcalus Manufacturing Co.*, 326 U.S. 249 (1945), compel the Court's rejection of licensee estoppel. Although the Court found the doctrine of assignor estoppel "inconsistent with the patent laws" as applied to the facts of the case, *id.* at 257-58, it is unclear why licensee estoppel – a different doctrine developed for different reasons – was undermined by the limitation that the Court placed on assignor estoppel in that case. Further, the Court's concern in *Scott Paper* was with the patent assignee's attempt to recapture by private agreement an expired patent's monopoly. *Id.* at 256. Such was not the Court's concern in *Lear*.

Finally, the antitrust cases on which *Lear* relied did not compel the Court's rejection of licensee estoppel as traditionally applied. The Court stated that cases such as *Sola Electric Co.* v. *Jefferson Electric Co.*, 317 U.S. 173 (1942), were "antithetic to the principles underlying [licensee] estoppel," *Lear*, 395 U.S. at 666; but *Sola* and the other cases cited by the Court dealt with the effect of the validity of patents on price-fixing clauses in licensing agreements, a question unrelated to the doctrine of licensee estoppel. *Sola* and similar cases recognize that such licenses become *per se* illegal price-fixing agreements as a matter of *antitrust* law if the patent is invalid. These cases are simply exceptions to the antitrust law rule that price fixing is acceptable if contained in a patent license.

In sum, none of the cases that *Lear* relied on compelled rejection of the doctrine of licensee estoppel as traditionally applied. The antitrust exception cases were afield; *Scott Paper*, at most, expressed a federal policy in favor of encouraging validity challenges in a different context; and both *St. Paul* and *Pope* in fact were examples of the licensee estoppel doctrine at work.

### 2. *Lear* Properly Overruled *Hazeltine*.

In *Lear*, the Court stated that *Automatic Radio Manufacturing Co.* v. *Hazeltine Research, Inc.*, 339 U.S. 827

(1950), in which it had most recently applied the doctrine of licensee estoppel, "should no longer be regarded as sound law with respect to its 'estoppel' holding." 395 U.S. at 671. The Court properly overruled *Hazeltine* because the Court's holding in that case was inconsistent with its holding in *Lear*.

In *Hazeltine*, a licensor sought royalty payments under the terms of a licensing agreement that provided for royalty payments that would be required whether or not the licensed invention was used. *See* 339 U.S. at 829-30. The licensee defended, arguing that, "notwithstanding the licensing agreement, [it] may contest the validity of the patents it is charged with using." *Id.* at 836. However, the Court rejected this argument based on "[t]he general rule * * * that the licensee under a patent license agreement may not challenge the validity of the licensed patent in a suit for royalties due under the contract." *Id.*

The holding of *Hazeltine* was too broad a statement of the rule – broader than the holding of *Lear* itself. In *Lear*, the licensee had voluntarily relinquished its claim to the benefits of the licensing agreement before asserting the patent's invalidity. At the very least, the Court in *Hazeltine* applied estoppel to the licensee without regard to whether the licensee had repudiated the benefit of the license. Thus, *Hazeltine* was an application of the "strong form" licensee estoppel rejected in *Lear*.

### C. *Lear* Should Be Limited To Similar Facts.

*Lear* was correctly decided because the "strong form" version of licensee estoppel endorsed by the California Supreme Court was inequitable and did not serve the purposes of the doctrine as traditionally understood. In support of its holding in *Lear*, the Court relied on federal policy in favor of encouraging patent validity challenges. *See* 395 U.S. at 670. The "strong form" version of licensee estoppel rejected in *Lear* indeed disserved this policy. Under that version of the doctrine, a licensee who became

convinced of the patent's invalidity would nevertheless – absent a valid termination – be unable to challenge the patent, even if he chose to repudiate the contract. Thus, the licensee could never, after signing the license and notwithstanding changed circumstances, opt out of the license and return to the position of a stranger to the patent. The Court correctly concluded that a rule, in effect requiring that licensees prospectively and irrevocably sign away their rights to challenge the validity of a licensed patent, is bad patent policy. *Lear* leveled the playing field by allowing a licensee who repudiates based on its belief that the patent is invalid (and thus that the license is unnecessary and improper) to assert the patent's invalidity as a defense in an action by the licensor.

The traditional doctrine of licensee estoppel, as opposed to the "strong form" version at issue in *Lear*, was equitable and well-supported. Traditional licensee estoppel imposes no irrevocable waiver of licensee challenges. Instead, the traditional doctrine simply requires licensees to choose between enjoying the benefits of the license and asserting the invalidity of the licensed patent. Under the doctrine, a licensee may choose either but not both, as the Federal Circuit properly refused to permit Petitioner to do here. Under the Federal Circuit's rule, the playing field remains level: a licensee may assert the invalidity of the licensor's patent, but only after forgoing the benefits that the patent license provides.

To be sure, encouraging patent invalidity challenges is a goal of federal patent law. But it is neither the only goal nor the overarching goal. "The stated objective of the Constitution in granting the power to Congress to legislate in the area of intellectual property is to 'promote the Progress of Science and useful Arts.'" *Kewanee Oil* v. *Bicron Corp.*, 416 U.S. 470, 480 (1974). Thus, for example, it is federal patent policy to reward inventors and to foster invention, including by encouraging the disclosure of inventions. *See id.* at 480-81; *see also Dawson Chem. Co.* v.

*Rohm & Haas Co.*, 448 U.S. 176, 221 (1980) (discussing "the policy of stimulating invention that underlies the patent system"). As the Federal Circuit has explained, allowing licensees in good standing to challenge the patents under license "yields undesirable results" because it "discourages patentees from granting licenses." *Gen-Probe, Inc.* v. *Vysis*, 359 F.3d 1376, 1382 (Fed. Cir. 2004). Such a rule would skew federal patent policy away from its overarching goal of encouraging invention and innovation.

The policy of encouraging invalidity challenges does not require that non-repudiating licensees be allowed to challenge the validity of licensed patents. Other avenues for challenging patent validity are available. First, the patent might be challenged by a non-licensee. Second, Congress in 1981 created a mechanism that allows individuals to request that the Patent and Trademark Office reexamine a patent based on prior art. *See* 35 U.S.C. §§ 302, 311(b). Thus, it is now substantially easier and less expensive to challenge the validity of a patent than it was when *Lear* was decided. Compared with the competing goal of encouraging innovation, the policy in favor of encouraging validity challenges is less in need of protection now than it was when *Lear* was decided.

The Court stated in *Lear* that its task was to "balance the claims of promisor and promisee in accordance with the requirements of good faith." *See Lear*, 395 U.S. at 670. Applying *Lear* so broadly as to permit licensee challenges without repudiation would not balance the interests of licensees and licensors in accordance with the requirements of good faith. Doing so would permit licensees in effect to inoculate themselves against infringement actions, and then, having limited their downside risk, immediately to seek to avoid their obligations under the parties' agreement altogether. "In other words, in this situation, the licensor would bear all the risk, while the licensee would benefit from the license's effective cap on

damages or royalties in the event its challenge to the patent's scope or validity fails." *Gen-Probe*, 359 F.3d at 1382.

Equitable and policy considerations thus support recognition of the continued validity of "traditional" licensee estoppel as a matter of federal patent law – and reading *Lear* as limited to its core holding.[5] That is just what the Federal Circuit did in stating that a licensee "cannot invoke the protection of the *Lear* doctrine until it (i) actually ceases payment of royalties, and (ii) provides notice to the licensor that the reason for ceasing payment of royalties is because it has deemed the relevant claims to be invalid." *Studiengesellschaft Kohle, m.b.H.* v. *Shell Oil Co.*, 112 F.3d 1561, 1568 (Fed. Cir. 1997).[6]

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[5] The negative incentive effects of *Lear*'s holding are substantial, and counsel strongly in favor of limiting it to similar facts. *See* John W. Schlicher, *Judicial Regulation of Patent Licensing, Litigation and Settlement Under Judicial Policies Created in Lear v. Adkins*, AM. INTELL. PROP. L. ASS'N, SELECTED LEGAL PAPERS, Vol. III, No. 1 (June 1985). As this paper shows, *Lear*'s rule – especially in its strong form – is economically inefficient, decreasing the output of licensees and increasing the deadweight loss of monopoly. While the rule increases patent invalidity challenges, the economic benefits therefrom are more than outweighed by the increased costs of the rule, including costs associated with (1) increased litigation, (2) decreased licensee productivity, (3) decreased rate of inventing, and (4) inefficient exploitation of inventions. *Id.* at 8-13.

[6] Other circuits have reached similar conclusions. *See Rite-Nail Packaging Corp.* v. *Berryfast, Inc.*, 706 F.2d 933, 936-37 (9th Cir. 1983); *Hull* v. *Brunswick Corp.*, 704 F.2d 1195, 1203 (10th Cir. 1983); *Am. Sterilizer Co.* v. *Sybron Corp.*, 614 F.2d 890, 897-98 (3d Cir. 1980); *PPG Indus.*,

(continued...)

## II. THIS CASE DOES NOT PRESENT A SUITABLE "CASE OR CONTROVERSY."

*Lear* did not address the question of jurisdiction under Article III or the Declaratory Judgment Act. As the Federal Circuit noted, "[i]n *Lear*, the licensee stopped paying royalties and the patentee sued for royalties; there was clearly a justiciable controversy, and that aspect was not an issue in *Lear*." Pet. App. 5. The Federal Circuit's conclusion that this case does not present an actual case or controversy is consistent with *Lear*.

In *Aetna Life Insurance Co.* v. *Haworth*, 300 U.S. 227 (1937), the Court first articulated the standards for a declaratory judgment action. The Court explained:

> The Declaratory Judgment Act of 1934, in its limitation to "cases of actual controversy," manifestly has regard to the constitutional provision and is operative only in respect to controversies which are such in the constitutional sense. The word "actual" is one of emphasis rather than of definition. Thus the operation of the Declaratory Judgment Act is procedural only. In providing remedies and defining procedure in relation to cases and controversies in the constitutional sense the Congress is acting within its delegated power over the jurisdiction of the federal courts which the Congress is authorized to establish.

*Id.* at 239-40. "The Declaratory Judgment Act allowed relief to be given by way of recognizing the plaintiff's right even though no immediate enforcement of it was asked."

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*Inc.* v. *Westwood Chems., Inc.*, 530 F.2d 700, 706, 708 (6th Cir. 1976).

*Skelly Oil Co.* v. *Phillips Petroleum Co.*, 339 U.S. 667, 671-72 (1950).

Petitioner seeks vindication of a substantive right that, absent its repudiation of the license agreement, it does not actually have. If *Lear* stands only for the proposition that a *repudiating* licensee may assert invalidity as a defense to an infringement action or a suit to recover royalties, and a non-repudiating licensee such as Petitioner has no such right, then Petitioner's "claim" is "foreclosed under the applicable substantive law," *Wilton* v. *Seven Falls Co.*, 515 U.S. 277, 282-90 (1995) (citation omitted), and Petitioner may not assert invalidity. To allow licensees to assert offensively in a declaratory judgment action that which they could not assert defensively in an action for royalties would impermissibly expand licensees' substantive rights. This would directly violate the Court's statement that the operation of the Declaratory Judgment Act is "procedural only." *Aetna*, 300 U.S. at 240.

Contrary to Petitioner's claim, the Court did not previously "decide[ ] the same jurisdictional issue before this Court today," Pet. Br. 16, in *Altvater* v. *Freeman*, 319 U.S. 359 (1943). *Altvater* did not concern the right of a non-repudiating licensee to assert invalidity claims. In *Altvater*, the Court held that a licensee could assert a counterclaim seeking a declaration relating to the validity of certain reissue patents. *See* 319 U.S. at 365-66. However, the reason the Court allowed the counterclaim was that the licensee was only paying the royalties "under compulsion of an injunction" from a prior case. *Id.* at 365. Indeed, the Court noted that the lower courts had found "that *the license agreement was terminated* on the surrender of the original patent and was not renewed and extended to cover the reissue patents." *Id.* at 364 (emphasis added). Therefore, it is clear that the licensee's obligation to continue paying royalties did not stem from the licensing agreement but from the injunction. As the Court made

clear, "[a] controversy was raging, even apart from the continued existence of the license agreement." *Id.* Thus, the Court's decision in *Altvater* did not touch on the question presented in this case; a question which the *Altvater* Court explicitly "put to one side" and declined to answer. *See id.*

Petitioner is invoking the Declaratory Judgment Act not to obtain an interpretation of the license agreement's terms, but to obtain advice about its potential legal exposure if it should repudiate the agreement and yet continue to practice the invention. That, however, is exactly the sort of question that private parties face all the time and for which they seek the advice of counsel. As the Eleventh Circuit has explained:

> Persons occupying positions of responsibility * * * often must make difficult decisions that can have adverse consequences for others. * * * Needless to say, the decisionmakers would benefit greatly by having guidance as to the potential legal ramifications of their decisions. Furnishing such guidance prior to the making of the decision, however, is the role of counsel, not of the courts.

*Hendrix* v. *Poonai*, 662 F.2d 719, 722 (11th Cir. 1981). For this reason, even if this case were thought to satisfy Article III, as implemented by the Declaratory Judgment Act, it would not be suitable for adjudication.

*Harris Trust and Savings Bank* v. *E-II Holdings, Inc.*, 926 F.2d 636 (7th Cir. 1991), is instructive. In that case, the trustee plaintiffs sought a declaration as to whether the appellee, a party to the indenture agreement at issue, was in default of that agreement. However, the district court held that it lacked Article III jurisdiction because the trustees "declined to declare an event of default under the terms of the Indentures," as they were free to do, and instead asked the court to determine whether a default had occurred. 722 F. Supp. 429, 441 (N.D. Ill. 1989). The

district court held that, because the trustees, "in effect, at all times ha[d] the power to create a controversy, but they ha[d] not yet done so," no actual controversy existed. *Id.*

The equities in favor of finding an actual controversy in *Harris Trust* arguably were substantial. As the Seventh Circuit explained, the decision whether to declare an event of default, if incorrect, likely would have exposed the trustees to suit. *See Harris Trust*, 926 F.2d at 638. Nevertheless, the court held that unless and until the trustees declared an event of default, the court lacked subject matter jurisdiction over the question. *See id.* at 640 ("the Trustees have declined to express an opinion on the merits[;] * * * that failure evidences the lack of a case or controversy").

Petitioner has the power to create an actual controversy but has not done so. In the same way that the trustees' failure to declare an event of default under the parties' agreement prevented the court from exercising its jurisdiction, the Petitioner's failure to repudiate its license prevents the federal courts from hearing this case. Of course, if Petitioner is wrong and Respondents' patent is valid, Petitioner would then be subject to an infringement suit (or a suit for royalties), but in this respect Petitioner is in the same position as the trustees in *Harris Trust*, who similarly would have faced substantial litigation exposure if they made the wrong choice. The mere fact that a party faces a difficult business decision does not confer jurisdiction on the federal courts. *See, e.g.*, *Crowley Co.* v. *United States*, 849 F.2d 273, 276 (7th Cir. 1988) ("You cannot go to a federal court for advice on the legality of a proposed course of action.").

## III. THE FEDERAL CIRCUIT'S RULE FURTHERS THE AIMS OF THE DECLARATORY JUDGMENT ACT AND PATENT POLICY.

From the earliest days of the Declaratory Judgment Act, the Court has consistently affirmed that federal courts are "under no compulsion to exercise th[eir] jurisdiction" in declaratory judgment actions. *Brillhart* v. *Excess Ins. Co.*, 316 U.S. 491, 494 (1942). Rather, through the Declaratory Judgment Act,

> Congress sought to place a remedial arrow in the district court's quiver; it created an opportunity, rather than a duty, to grant a new form of relief to qualifying litigants. Consistent with the nonobligatory nature of the remedy, a district court is authorized, in the sound exercise of its discretion, to stay or to dismiss an action seeking a declaratory judgment before trial or after all arguments have drawn to a close. * * * In the declaratory judgment context, the normal principle that federal courts should adjudicate claims within their jurisdiction yields to considerations of practicality and wise judicial administration.

*Wilton*, 515 U.S. at 288 (footnote omitted).

In the words of the Federal Circuit, the purpose of the Declaratory Judgment Act is to

> enable a person who is reasonably at legal risk because of an unresolved dispute, to obtain judicial resolution of that dispute without having to await the commencement of legal action by the other side. It accommodates the practical situation wherein the interests of one side to the dispute may be served by delay in taking legal action.

*BP Chems. Ltd.* v. *Union Carbide Corp.*, 4 F.3d 975, 977 (Fed. Cir. 1993).

By entering into licensing agreements, licensors give up a number of important rights, including the right to exclude the licensee from using the claimed invention and, in the case of use, to sue for treble damages, among other things. If the licensee is nevertheless allowed to seek to invalidate the patent, then the licensee has effectively given up nothing. Under this regime, "the licensor would bear all the risk, while licensee would benefit from the license's effective cap on damages or royalties in the event its challenge to the patent's scope or validity fails." *Gen-Probe*, 359 F.3d at 1382. Therefore, to allow the licensee to sue the licensor, even while retaining the protection of the license, would undermine rather than serve the principle of equality that underlies the Declaratory Judgment Act.

"The factors relevant to wise administration here are equitable in nature." *Kerotest Mfg. Co.* v. *C-O-Two Fire Equip. Co.*, 342 U.S. 180, 183 (1952). Those factors here militate in favor of declining jurisdiction even if Article III and the Act permit a federal court to exercise jurisdiction. *See, e.g.*, *Wilton*, 515 U.S. at 288; *Hewitt* v. *Helms*, 482 U.S. 755, 762-63 (1987); *Pub. Affairs Assocs., Inc.* v. *Rickover*, 369 U.S. 111, 112 (1962); *Brillhart*, 316 U.S. at 494 (Frankfurter, J.); *Great Lakes Dredge & Dock Co.* v. *Huffman*, 319 U.S. 293, 300 (1943) (Stone, C.J.). Accordingly, the Court could affirm the Federal Circuit's judgment on equitable and prudential grounds and leave the Article III question to the future. *See Elk Grove Unified Sch. Dist.* v. *Newdow*, 542 U.S. 1, 11-18 (2004) (reversing for lack of prudential standing and avoiding Article III issue on which review had been granted); *see generally J. E. Riley Inv. Co.* v. *Comm'r*, 311 U.S. 55, 59 (1940) ("Where the decision below is correct it must be affirmed by the appellate court though the lower tribunal gave a wrong reason for its action."); *Chevron U.S.A., Inc.* v. *NRDC, Inc.*, 467 U.S. 837, 842 (1984) ("this Court reviews judgments, not opinions").

## CONCLUSION

For the foregoing reasons, the judgment should be affirmed.

Respectfully submitted,

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IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner*,

v.

GENENTECH, INC., *et al.*,

*Respondents.*

**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## BRIEF OF AMERICAN INTELLECTUAL PROPERTY LAW ASSOCIATION AS *AMICUS CURIAE* SUPPORTING RESPONDENTS

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## BRIEF OF AMERICAN INTELLECTUAL PROPERTY LAW ASSOCIATION AS *AMICUS CURIAE* SUPPORTING RESPONDENTS

### STATEMENT OF AMICUS INTEREST

The American Intellectual Property Law Association (AIPLA) has no interest in any party to this litigation or stake in the outcome of this case, other than its interest in seeking a correct and consistent interpretation of the law affecting intellectual property.[1] AIPLA is a voluntary bar association of over 16,000 members who work daily with patents, trademarks, copyrights, trade secrets, and the legal issues that

[1] In accordance with Supreme Court Rule 37.6, AIPLA states that this brief was not authored, in whole or in part, by counsel to a party, and that no monetary contribution to the preparation or submission of this brief was made by any person or entity other than AIPLA or its counsel.

intellectual property presents. AIPLA's members include attorneys in private and corporate practice and in government service who secure, license, enforce, and defend against enforcement of intellectual property rights. As part of its central mission, AIPLA is dedicated to encouraging the healthy development of rules governing patent rights. Accordingly, AIPLA has a vital interest in the issue presented by this case, which will have a far-reaching impact on how patent rights are shared, challenged, and enforced. The outcome is of critical concern to AIPLA because its members regularly counsel and represent parties involved with patent licensing and litigation.

Counsel of record for all parties consented to the filing of this brief pursuant to Supreme Court Rule 37.3(a).

## SUMMARY OF ARGUMENT

The Federal Circuit correctly held that jurisdiction did not exist under the Declaratory Judgment Act, 28 U.S.C. § 2201, because the parties' dispute lacked sufficient immediacy and genuine adversity to satisfy the requirement of Article III. To affirm in this case, however, the Court need not rule that a licensee must necessarily breach the license before a declaratory judgment action can be maintained. The critical Article III elements of a live controversy, *i.e.*, a concrete and immediate dispute, may also exist if the licensor and licensee engage in a legitimate debate over the validity or scope of the licensed patent rights after the license is executed, due to, for example, an unforeseen change in circumstances, and the licensor makes clear that it will promptly sue if the licensee fails to make timely payments according to its interpretation of the license. In that circumstance, there would also be mutuality of recourse to resolve the dispute. The necessary threat never occurred in this case, precluding petitioner from satisfying a constitutionally sufficient jurisdictional test.

Another example illustrates that a breach of a license is not necessary to support jurisdiction. A patent and pending applications may be licensed on the basis of the licensee's understanding that the patent covers only a certain portion of its products. If one of the pending applications unexpectedly issues with broad claims that cover all of the licensee's products and that the licensee rightfully believes are invalid, the licensee should be able to protest the payment of additional royalties. If the patentee responds to the licensee by insisting that royalties be paid on all products and threatens suit if they are not, the licensee is at risk if it does not increase its payment corresponding to all of the products. This type of circumstance can provide an immediate threat justifying a declaratory judgment action even if the licensee continues to pay royalties at the greater amount.

Petitioner's proposed rule, by contrast, grants licensees an absolute right to challenge the validity of patents they have voluntarily licensed without placing themselves at risk, allowing licensees to retain the shield of a license to protect them from an infringement suit, while they use the sword of a declaratory judgment action to invalidate the very patents they agreed to license. Such a rule would violate basic constitutional principles that limit the Declaratory Judgment Act to controversies of sufficient immediacy between parties with genuinely adverse legal interests. *Md. Casualty Co.* v. *Pac. Coal & Oil Co.*, 312 U.S. 270, 273 (1941). Petitioner's rule would extend patent licensees a unilateral option to attack the licensed patent when the licensor makes no threats and is barred by the license from a mutual action against the licensee. Allowing patent licensees to bring risk-free challenges to patent validity would increase litigation, encourage questionable licensing tactics, and disrupt the settled expectations of patent licensors.

In applying the constitutional requirements of immediacy and mutuality to declaratory judgment jurisdiction, the

Federal Circuit properly considered whether the plaintiff has a reasonable apprehension of being sued by the named defendant. This is not a bright-line test that always requires a breach of the patent license; instead, the analysis allows the "totality of the circumstances," in an appropriate case, to justify a finding of jurisdiction.

As the Federal Circuit correctly observed, permitting a declaratory judgment action to proceed in this case would create an imbalance that "distorts the equalizing principles that underlie the Declaratory Judgment Act." Pet. App. 7a. By contrast, all relevant constitutional and policy concerns are satisfied by requiring a live dispute, *e.g.*, a challenge to the patent communicated by the licensee to the licensor, coupled with the licensor's threat of suit if the licensee fails to abide by the license in a manner sought by the licensor.

## ARGUMENT

### I. THE CONSTITUTIONAL REQUIREMENTS OF IMMEDIACY AND GENUINE ADVERSITY CANNOT BE SATISFIED WITHOUT AN IMMEDIATE THREAT TO THE LICENSEE.

The Declaratory Judgment Act satisfies the Constitution's Article III limits on judicial power by creating jurisdiction only for cases involving an "actual controversy." *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227 (1937) (construing Declaratory Judgment Act of 1934). In *Maryland Casualty Co.*, 312 U.S., at 273, the Court explained that disputes in declaratory judgment actions must be immediate, which is demonstrated at least in part by the fact that the declaratory judgment defendant could have brought an affirmative claim:

> "Basically, the question in each case is whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of *sufficient immediacy* and reality to warrant the issuance of a declaratory judgment. It is

immaterial that frequently, in the declaratory judgment suit, the positions of the parties in the conventional suit are reversed; the inquiry is the same in either case." (citations omitted) (emphasis supplied).

The immediacy requirement is implemented in the lower courts, including the Federal Circuit, by the well-established "reasonable apprehension of suit" test that was applied in this case and has been relied upon since the 1960s. *See, e.g., Teva Pharms. USA, Inc.* v. *Pfizer, Inc.*, 395 F.3d 1324, 1335 (CA Fed.), cert. denied, 126 S.Ct. 473 (2005); *C.R. Bard, Inc.* v. *Schwartz*, 716 F.2d 874, 879 (CA Fed. 1983); *Societe de Conditionnement en Aluminium* v. *Hunter Engineering Co., Inc.*, 655 F.2d 938, 944-945 (CA9 1981); *Japan Gas Lighter Assn. v. Ronson Corp.*, 257 F.Supp. 219, 237 (NJ 1966) (generally credited with formulating test). The "reasonable apprehension of suit" inquiry asks whether the putative declaratory judgment plaintiff had a reasonable apprehension of an imminent suit. *Teva Pharms.*, 395 F.3d, at 1335. A substantial body of law has evolved based on this test, which is aimed directly at addressing the constitutional requirement of an "actual controversy." See, *e.g.*, *id.*, at 1335-1336.

Petitioner seeks a rule that would deem all disputes about licensed patents to be immediate, and thus justiciable, regardless of whether the licensor has taken any affirmative action to suggest a live threat to the licensee. The constitutional requirement of immediacy, however, mandates a focus on whether the licensee truly faces an immediate threat. Although a license is normally inconsistent with such a threat, subsequent developments could conceivably create a sufficient threat to permit an exercise of jurisdiction. By properly focusing on the threat to the licensee, the Federal Circuit's reasonable apprehension test is balanced and adaptable.

Because a license is often an agreement to resolve existing disputes over patent rights, it is reasonable to preclude a licensee from challenging the licensed patents until

the parties' subsequent interactions establish an immediate and concrete dispute. If, for example, an unforeseen change of circumstances reasonably causes the licensee to believe that it need not continue to pay royalties because the patent is invalid or does not cover the licensee's products, that party is not under a threat until it raises the issue with the licensor and is met with conduct or actions indicating that, if the licensee ceases paying the disputed royalties, it will face a prompt infringement or contract suit. In that event, the licensee is under a threat and an immediate and real dispute exists. The existence of the real dispute does not require confirmation by the licensee actually breaching the license.

This application of the immediacy requirement forces the parties to join issue before allowing the licensee to seek court intervention, thus promoting the extrajudicial resolution of disputes and deterring the premature filing of lawsuits. A licensor will not always be willing to litigate to defend the validity of its patent. Allowing a suit to proceed before a true dispute exists, as petitioner would have it, would give the licensee the ability to launch an unannounced attack on a licensed patent whenever and wherever it chooses.

### A. The Record in This Case Evidences a Complete Lack of Immediacy.

This case evinces no "immediacy"—or "reasonable apprehension of suit," to use the standard formulation developed by the lower courts. Petitioner's voluntary decisions to enter into the license and to pay royalties on the license eliminated any risk that Genentech would—or could—enforce the patent against it. Because Genentech could not bring suit, and did not threaten to do so, there was no immediacy to petitioner's desire to litigate the validity of the Cabilly II patent.

Petitioner does not directly address the absence of immediacy. It does not explain, for example, how a suit brought after a delay of over a year from the date payment

was sent "under protest," J.A. 426, could arise from an immediate dispute, or how the period of immediacy could end—if ever. In sharp contrast, under the reasonable apprehension test consistently applied by the Federal Circuit, the threatening actions of the patentholder provide a concrete basis to measure when the dispute is sufficiently ripe. But if the declaratory judgment plaintiff need not have a reasonable apprehension of suit, as petitioner contends, Pet'r Brief 23-25, the putative immediacy of any validity dispute would have no boundaries and could exist for the remaining life of the licensed patent. Such an unripe and one-way "controversy" cannot meet the constitutional standard of an immediate and real dispute.

### B. The Court's Precedent Does Not Support a Conclusion of Immediacy on These Facts.

None of the decisions invoked by petitioner establishes that this case satisfies the constitutional immediacy requirement. For example, in *Lear, Inc.* v. *Adkins*, 395 U.S. 653, 660 (1969), the patentee had sued the licensee for failure to pay royalties and only then did the licensee counter with its invalidity defense. Thus, the dispute was not only immediate, it was already underway when the invalidity declaratory judgment counterclaim was introduced. Put simply, the licensor's action against the licensee unmistakably created the required immediacy.

Petitioner also relies heavily upon *Altvater* v. *Freeman*, 319 U.S. 359 (1943). But in *Altvater*, like *Lear*, the party seeking to bring a declaratory judgment counterclaim of patent invalidity had been sued first. Thus, an action had been already initiated against the party bringing the declaratory judgment claim, obviously engendering an immediate and ripe dispute. Indeed, in *Altvater*, immediacy was established by the fact that the invalidity counterclaim accompanied an ultimately successful counterclaim, which confirmed that the parties' license had terminated. 319 U.S.,

at 362 ("[T]he license agreement terminated with the surrender of the original patent in 1936."). Thus, in contrast to this case, the dispute over the patents was ripe because there was *no* license at all precluding an infringement claim, and by bringing suit the patentee had made clear that it sought to enforce its patents.

The fundamental distinction between *Altvater* and this case is that here a valid license unquestionably prevents an infringement suit, whereas in *Altvater* the license no longer existed.[2] Further, the injunction pursuant to which royalties were being paid was being eliminated because it was unquestionably based on a patent that no longer existed, leading this Court to conclude that "the required payment of royalties under that decree does not establish the absence of a controversy." *Id.*, at 365 n.5.

The contract cases cited by petitioner are no more persuasive. Although one of the purposes of the Declaratory Judgment Act is to resolve concrete and immediate disputes over contract rights, that does not make all contract-related issues immediate and thus justiciable. For example, in *Highsmith* v. *Chrysler Credit Corp.*, 18 F.3d 434, 437 (CA7 1994), the Seventh Circuit found a dispute regarding a contract termination clause insufficiently "imminent" to support a declaratory judgment claim when the party attempting to bring the declaratory judgment claim had not terminated the contract or threatened to do so.[3]

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[2] Petitioner's brief wrongly assumes that the license in *Altvater* remained viable, and thus its analysis misses this critical distinction.

[3] The United States also relies upon decisions holding that a party may challenge a statute before it is enforced if there is a genuine risk of enforcement. Brief for the U.S. 9 (citing *Steffel* v. *Thompson*, 415 U.S. 452, 459 (1974)). That line of cases makes clear that the risk of enforcement must be such that the complaining party seeking to bring the declaratory judgment action is "immediately in danger" of facing enforcement. *City of Los Angeles* v. *Lyons*, 461 U.S. 95, 102 (1983). It

In sum, this case lacks the constitutionally required immediacy. Because petitioner paid all royalties possibly due under the license and Genentech never threatened to bring suit, there was no immediate dispute.

## II. THE CONSTITUTIONAL REQUIREMENT OF IMMEDIACY CANNOT BE MET WHEN THE DISPUTE LACKS MUTUALITY.

In *Aetna,* the Court ruled that the Declaratory Judgment Act was constitutional because the declaratory judgment claim was simply the mirror image of the affirmative and unquestionably justiciable claim that the declaratory judgment defendant had threatened and could have brought. *Aetna*, 300 U.S., at 244 ("[T]he character of the controversy and of the issue to be determined is essentially the same whether it is presented by the insured or the insurer."). The bilateral nature of the dispute made it immediate and concrete.

The characteristic of mutuality is ensured by requiring the parties to actually engage concerning their dispute—creating an immediate threat—before the licensee can file a declaratory judgment action. For example, if the licensee were to threaten to challenge the patent, the licensor would be in a position to file a declaratory judgment action to confirm the licensee's obligation to pay under the license in a venue of its choosing. Thus, each side should have an equal opportunity to seek relief.

Such mutuality is central to the Declaratory Judgment Act, which was designed to ensure that both sides to a dispute have an opportunity to seek relief from the court system.

> "The Declaratory Judgment Act was designed to relieve potential defendants from the Damoclean threat of impending litigation which a harassing adversary might brandish, while initiating suit at his leisure—or never.

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cannot be said on this record that there was an immediate danger that Genentech would file suit.

The Act permits parties so situated to forestall the accrual of potential damages by suing for a declaratory judgment, once the adverse positions have crystallized and the conflict of interests is real and immediate." *Japan Gas Lighter*, 257 F.Supp., at 237 (citing *Md. Casualty Co.*, 312 U.S., at 273).

## III. In the Absence of a Live Threat of Liability, a Licensee's Challenge to the Patent Cannot Meet the Constitutional Requirement of Adversity.

An additional requirement to meet the constitutional standard of justiciability is genuine adversity of the parties' legal interests. *Md. Casualty Co.*, 312 U.S., at 273. In a patent licensing situation, however, there is no reliable basis for assuming that genuine adversity exists, and there are dangers in any bright-line rule that might rely on the mere appearance of adversity.

In *Lear*, the Court recognized that a licensee and licensor often share a common interest in the strength of the licensed patent rights. *Lear*, 395 U.S., at 669. *Lear* described the typical interest a licensee has in a license, noting that the licensed patent can "deter others from attempting to compete with the licensee." *Ibid.* If the license is exclusive, it is obvious that the licensee benefits if the patent is effective. However, the Court explained that a licensee has an interest in the strength of the patent even if the license is non-exclusive: "Even in the case of nonexclusive licenses, however, competition is limited to the extent that the royalty charged by the patentee serves as a barrier to entry." *Id.*, at 669 n.16; see also Dreyfuss, Dethroning *Lear*: Licensee Estoppel and the Incentive to Innovate, 72 Va. L. Rev. 677, 703-706 (1986) ("Indeed, so long as the patentee does not extract all the extra profit the licensee can charge, a licensee will almost always have as strong an interest as a patent

challenge and will therefore not function in the public interest.").

In light of these interests, the licensee's required royalty payments may present only the appearance of adversity to the licensor, rather than the genuine adversity mandated by Article III. This adversity question is not answered by either *Lear* or *Altvater* because the declaratory judgment claimants were already involved in hotly contested litigation. Moreover, in *Lear,* the licensee had repudiated the licensing agreement and was being sued for nonpayment under the license, and in *Altvater,* the license was terminated by virtue of reissue of the subject patents.

The Court should not adopt petitioner's ill-conceived jurisdictional rule and open the door to friendly lawsuits between licensees and licensors that are simply designed to strengthen the patent rights they share. Such friendly litigation is the antithesis of a true case or controversy. A declaratory judgment "challenge" that *reaffirms* the validity of a valuable patent will quite often be in the interest of a licensee. Courts would have no reliable way of identifying the true motives of licensees when they file a declaratory judgment action, especially because those motives may be mixed or shifting.

The mere risk of this kind of manipulation of the courts is enough to cast doubt on a rule that permits risk-free validity challenges. On the other hand, once the licensee has been threatened by the licensor, true adversity is assured and the integrity of the adjudication is protected.

## IV. Allowing Risk-Free Challenges to Patents by Licensees Creates the Wrong Incentives.

Licenses are the primary way that patent rights are shared. Promoting consensual licensing activity is generally beneficial and is one way to avoid wasteful disputes and litigation. The rule proposed by petitioner destabilizes licensing activity and promotes litigation and disputes.

### A. Risk-Free Challenges Undermine Trust and Promote Increased Litigation.

Trust is important to healthy negotiations of any kind. Allowing licensees to attack freely the validity of licensed patents on a risk-free basis will undermine trust and feed suspicion. Most obviously, licensees will have an incentive to challenge licensed patents in court far more often. Typically, the only cost to the licensee of such an approach will be attorneys' fees with a business upside of: (1) strengthening the licensed patent if it withstands a validity challenge; (2) avoiding royalties entirely if the patent does not withstand a validity challenge, or; (3) perhaps, most commonly, reducing royalties owed due to a settlement of the challenge to the patent.

Petitioner's rule would not only promise more litigation from licensees, but it would also inspire patent owners to litigate more often. Rather than face a series of negotiations, suits, and renegotiations with its licensees, licensors would more likely opt for the finality of a conclusive judgment that protects from attacks on the validity of their patents. A patent owner entering into a license before litigating the validity of its patent would effectively disarm itself by foregoing the right to pursue an infringement claim while remaining exposed to suit by the licensee. Consensual licensing would be less desirable than it is now. Licensors would also likely increase the price of licenses to compensate for the risk of repeated renegotiations, with the higher costs to licensees being passed along to the public. See Goodman, Patent Licensee Standing and the Declaratory Judgment Act, 83 Colum. L. Rev. 186, 211 (1983) (noting that passing along higher license costs "diminish[es] the benefits the public currently receives from the patent system").

### B. Risk-Free Challenges Encourage Inefficient and Questionable Licensing Tactics.

Petitioner does not address the undesirable incentives that would flow from the rule it promotes. The United States, on the other hand, concedes that licensors would be placed in a difficult position, see Brief for the U.S. 28, and its response on that key point only heightens concern about petitioner's rule.

Specifically, the United States argues that licensors can ameliorate the effects of petitioner's rule through a host of licensing tactics. The United States posits that while the law bars licensors from having licensees contract away their right to challenge the validity of a patent, licensors can include provisions that make the decision to challenge a licensed patent painful. *Ibid.*

For example, the United States suggests that "a licensor may be able to make the filing of a declaratory judgment action a basis for terminating the license, changing the royalty rate to a specified higher rate, or otherwise adjusting the pre-challenge terms." *Ibid.* The United States thus provides licensors with a menu of terms they can include in licenses to deter, and even punish, declaratory judgment invalidity actions. Yet, the United States concedes that the tactics it proposes would be legally questionable:

> "While the enforceability of such provisions is an open question in light of the strong public policy favoring patent challenges as reflected in *Pope* and *Lear*, those decisions do not necessarily entitle a licensee both to challenge the licensed patent and to retain all the benefits of his license agreement, if the agreement expressly provides otherwise." *Ibid.* (citation omitted).

Petitioner's rule would set off a new round of disputes about what licensors can do to counteract the licensees' power to

attack the validity of patents in what would otherwise be a risk-free way.

The United States also suggests that licensors could demand lump-sum up-front royalties in lieu of royalties paid as traditional running royalties. *Id.*, at 29. The common running royalty requires the licensee to pay royalties on an ongoing basis as a percentage of the sales price of its products. The United States reasons that licensees that pay for patent rights upfront and in full, rather than by owing running royalties, will be discouraged from challenging the licensed patent through declaratory judgment actions. *Ibid.* ("Patentees concerned about potential litigation could, for example, require prospective licensees to purchase a fully paid up license.").

Although the United States is correct that the petitioner's rule would encourage lump-sum up-front royalties, its proposal of fully paid-up payments distorts the common commercial desire to use the often favored running-royalty approach. AIPLA, whose members frequently engage in negotiating patent licenses, can attest to the fact that licensing parties more frequently prefer running royalties. Under that royalty model, the payments for the use of technology correspond to the extent of use of the technology over time. Declaratory judgment jurisdictional prerequisites should not disrupt the market's structuring of economic relationships in this way.

In addition, the lump-sum payment approach would undermine the very policy that the United States asks the Court to endorse. Specifically, the United States urges the Court to motivate licensees to invalidate bad patents even at the cost of lowering the bar as to what is justiciable as an immediate and concrete dispute. However, licensees have no incentive to challenge licensed patents when they have already paid for them fully—even if they learn later that they

are in fact invalid. To the contrary, such licensees have every incentive to see that their paid-for rights are preserved.

If the petitioner's rule were accepted, licensors may attempt to rebalance their negotiating power by including the questionable licensing terms identified by the United States—and presumably others. A new period of uncertainty in which the enforceability of these different terms is tested would be costly. Moreover, these terms are designed to discourage the very validity challenges that the Court is being asked to endorse. The uncertainty and brinksmanship in licensing practice that would accompany petitioner's rule are undesirable and should be avoided.

Meanwhile, many avenues permit parties to challenge the validity of a patent without implicating the problems that would accompany petitioner's rule. For example, even if a party made a business decision to license and pay royalties under a patent of questionable validity, that party may still indirectly challenge the patent's validity by requesting that the Patent Office reexamine the patent.[4] See Fisher, The Licensee's Choice: Mechanics of Successfully Challenging a Patent Under License, 6 Tex. Intell. Prop. L.J. 1, 45 (1997) ("The existence of a license agreement does not affect the licensee's right to file for reexamination.").

Petitioner's rule threatens to usher in a new and undesirable era in patent licensing which would disrupt not only future licensing activities, but also the expectations of existing licensors. Based on settled law over the last two decades, licensing parties would not have expected that licensees could file risk-free challenges to the patents they license. Petitioner's rule would likely cause a surge in declaratory judgment claims and rounds of license

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[4] Indeed, Petitioner has taken advantage of that very opportunity in this case. The Patent Office granted the request in July 2005, and the reexamination proceeding is still pending.

renegotiations. On the other hand, if the Court upholds the Federal Circuit's requirement for a reasonable apprehension of suit, the Court would preserve the fair balance currently existing among parties to patent licensing agreements.

## CONCLUSION

The Court should affirm the decision of the Federal Circuit.

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IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

*v.*

GENENTECH, INC., ET AL.

*Respondents.*

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

## BRIEF OF THE BOSTON PATENT LAW ASSOCIATION AS *AMICUS CURIAE* IN SUPPORT OF GENENTECH, INC., ON THE MERITS

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## INTEREST OF *AMICUS CURIAE*

The Boston Patent Law Association ("BPLA") is a non-profit association of intellectual property professionals that provides programs and forums for the exchange of ideas and information about patent and other intellectual property rights. The BPLA favors a healthy and balanced patent system, which in turn fosters innovation and bolsters the American economy. Departing from the case or controversy requirement of Article III, however, may ultimately upset the balance in the patent system and, correspondingly, discourage innovation and technology licensing. As such, this case evokes the BPLA's interest.[1]

## SUMMARY OF ARGUMENT

The Court of Appeals for the Federal Circuit correctly determined that MedImmune's mere desire to challenge the Cabilly II patent while still retaining the benefits of its license with Genentech did not create an actual controversy sufficient to trigger Article III jurisdiction. The BPLA agrees with the Federal Circuit's reasoning in this and other cases holding that a licensee in good standing may not challenge the licensed patents in court. *See, e.g., Gen-Probe, Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir. 2004); *MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005).

Rather than repeat or bolster the Federal Circuit's legal analysis in these cases, the BPLA instead wishes to dispel the impression, advanced by MedImmune, that the patent system is somehow off-kilter, that patents are unsound, and

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[1] Pursuant to Supreme Court Rule 37.6, no party or its counsel authored any part of this brief. No person or entity, other than the BPLA and its counsel, Bromberg & Sunstein LLP, contributed money for the preparation or submission of this brief. The parties have consented to the filing of this *amicus* brief. The consent letters have been lodged with the Court.

that the mere hint of an invalid patent justifies a departure from the Article III actual controversy requirements.

In short, contrary to MedImmune's contentions, there is no plague of bad patents threatening licensing, competition, or innovation. As such, there is no need to make an exception to the Article III controversy standard as a way to address a perceived but unsubstantiated problem with the quality of patents. On the other hand, writing a new rule that allows licensees in good standing to challenge licensed patents will upset the balance between licensors and licensees, create uncertainty, and thus cause intellectual property owners to lose faith in licenses as a valid means of (a) profiting from innovation and (b) settling infringement disputes efficiently.

Thus, the BPLA's argument is two-fold. First, the patent system is not broken. Statistics reveal that issued patents are generally sound and deserve their statutory presumption of validity. Accordingly, there is no policy reason to allow licensees in good standing to challenge patents. And even if the statistics were otherwise, even if there were a plague of bad patents infesting the economy, the response should come from Congress or the Executive branch, not from this Court. For example, Congress and the United States Patent and Trademark Office ("PTO") could takes steps to improve patent examination so that fewer defective patents issue.

Second, if anything, public policy justifies the Federal Circuit's holding. A policy favoring settlement of litigation through licensing trumps a policy of removing allegedly invalid patents from the economy. Technology licensing generates billions of dollars and is increasingly important to the American economy. Licensing also benefits consumers by ensuring that innovative products, life-saving drugs and medical devices, and other inventions make their way to the market. A ruling that allows an intellectual property user to take a license only to turn around and challenge the

underlying patent when it becomes expedient to do so, however, will ultimately devalue licenses, making them less certain and less efficient as a means for balancing the needs of intellectual property owners and users.

## ARGUMENT

### I. PATENTS ARE SOUND; THUS, THERE IS NO POLICY REASON FOR UNDERMINING THE ARTICLE III CONTROVERSY STANDARD

There is nothing to suggest that a plague of invalid patents threatens the U.S. economy and that, as MedImmune contends, there is a crisis somehow justifying a ruling that, for the first time, would allow licensees in good standing to challenge allegedly invalid patents. Just the opposite holds true. Statistics suggest that the PTO is doing its job and is, on the whole, issuing valid patents. Thus, there is no urgent reason to disturb the Federal Circuit's refusal to depart from the actual controversy requirement. But even if there were a problem with patent quality, the fix should come from Congress, not from this Court.

#### A. Patents Are Generally Sound

According to John Dudas, Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, the notion that the patent system is broken is based on misperception, not on fact. *See* Neil E. Graham, *Perception Gap Hindering Efforts to Improve Patent System, Dudas Says*, 71 Pat. Trademark, & Copyright J. 374 (2006). In fact, patent quality is improving. For example, Dudas corrects a misperception that the increasing number of patent applications has led to decreasing patent quality. Statistics show that the percentage of applications granted has actually decreased (suggesting that the PTO is being more selective) while the number of patent examiners

has increased to keep up with demand. *Id.* Moreover, despite a perception that up to 40% of all patents are overturned in court, "less than 1/20th of one percent of all patents that issue are actually overturned in court." *Id.*

Congress has determined that U.S. patents are presumed valid. 35 U.S.C. § 282. That presumption of validity stems, in part, from the presumption that a government agency, such as the PTO, does its job well. *American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350, 1359 (Fed. Cir. 1984). That presumption is well deserved.

A review of the patent application process shows that PTO examiners are far from bored clerks rubber-stamping applications until the clock strikes five. Contrary to MedImmune's contention, the PTO does not grant every application it receives. Rather, the PTO does its job conscientiously and scrutinizes each application for compliance with all statutory requirements for patentability.

Specifically, when an inventor files an application for patent, the PTO assigns the application to an examiner versed in the technology of the claimed invention. After reviewing the application and searching for relevant prior art, the examiner typically rejects the application for one or more alleged defects and states his or her reasons in a so-called "office action." A patent application often receives not just one but two rounds of office actions. To overcome a rejection, the applicant must justify the patentability of the invention (*e.g.*, by distinguishing prior art cited by the examiner). In some instances, the applicant must narrow the scope of the claims to overcome the rejection.

The PTO issues office actions rejecting patent claims roughly 90% of the time. Indeed, a patent almost never issues on the first pass. *See, e.g.*, Andrew T. Zidel, *Patent Claim Construction in the Trial Courts: A Study Showing the*

*Need for Clear Guidance from the Federal Circuit*, 33 Seton Hall L. Rev. 711, 717–18, n.49 (2003) (giving an overview of patent prosecution and positing that claims are initially rejected 75–100% of the time); Procedure for Obtaining U.S. Patent, *at* http://www.angenehm.com/pat_faqs4.html (last visited July 23, 2006) ("The USPTO examines the application and in about 90% of the cases finds reason why the patent should not issue"); Larry J. Guffey, *Business Method Patents: What They Are — Why Clients and Service Providers Should Care*, 33 Md. B.J., July/Aug. 2000, at 25, 28 (2000) (initial rejection of patent claims occurs about 80% of the time and there are usually two rounds of office actions per application); Ronald E. Smith, The Ten Commandments of Inventing, *at* www.library.okstate.edu/patents/tencmds.htm (last updated June 26, 2006) ("According to PTO statistics, about 90 percent of all patent applications are initially rejected").

Not every application results in a patent. Rather, contrary to MedImmune's claim that 74% to 98% of all patent applications are granted, currently only about 50% of applications mature into patents. As seen in Figure 1 below, the percentage of patents granted has declined over the years. Moreover, as seen in Figure 2 below, the number of patents granted has leveled off at 180,000 per year, even as the number of applications has risen.[2]

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[2] The BPLA based Figures 1 and 2 on statistics compiled by the PTO. *See* U.S. Pat. & Trademark Office, *U.S. Patent Statistics Chart: Calendar Years 1963–2004*, *available at* http://www.uspto.gov/go/taf/us_stat.htm (last visited July 23, 2006) [hereafter *USPTO Patent Statistics*].

Figure 1. Percentage of Patents Granted Per Year

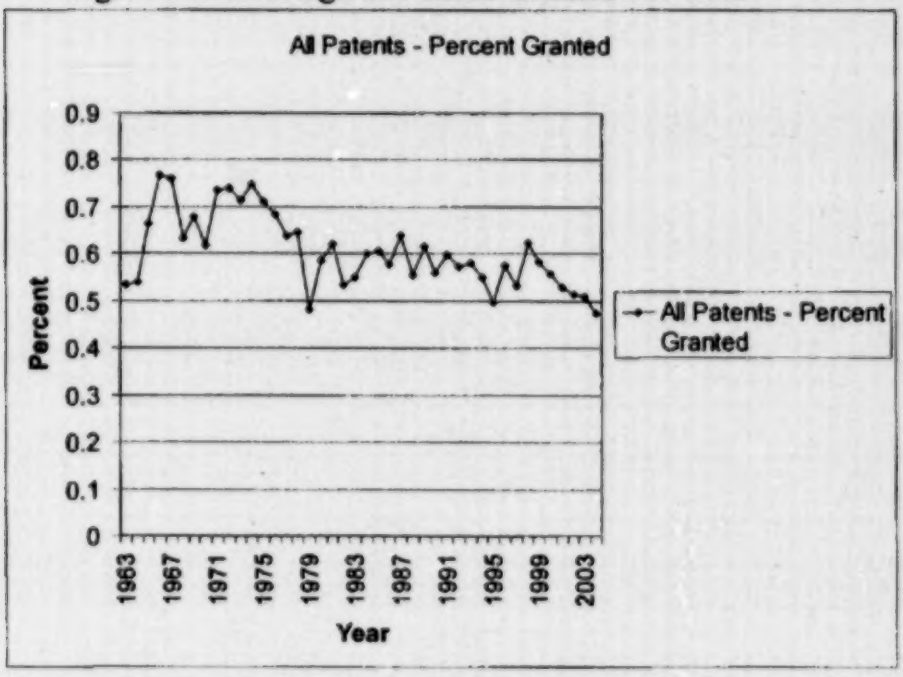
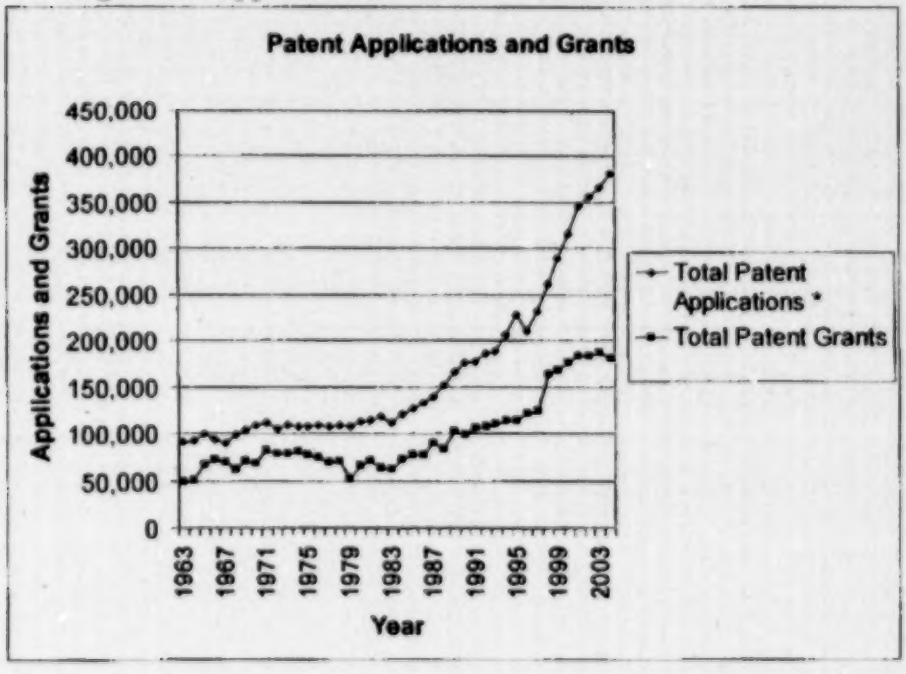



Figure 2. Applications and Grants Per Year




These trends suggests that the PTO is exercising appropriate selectivity. Indeed, the PTO appears to be getting stingier in granting patents. Perhaps, given the emergence of better

prior art searching capabilities (specifically, the use of computer and Internet prior art databases), the PTO is becoming even better at its job of rigorously examining patent applications.[3]

In some industries, the percentage of patent grants is significantly below the 50% level. For example, business method patents, frequently a target of criticism (most recently in the *eBay v. MercExchange* case), have been maligned as too easy to obtain. In March 2000, the PTO moved to address such criticism and thus hired and trained additional examiners and instituted a second level of patent review. *See* John R. Allison & Emerson H. Tiller, *The Business Method Patent Myth*, 18 Berkeley Tech. L.J. 987, 995 (2003). As a result of these and other improvements at the PTO, the percentage of business method patents granted fell from 56% to 36% in one year alone. *Business Method Patents: Hearing Before the Subcomm. on Courts, the Internet, and Intellectual Property of the H. Comm. on the Judiciary*, 107th Cong. 58 (2001) (statement of Ronald E. Myrick, President, Intellectual Property Owners Association). Under Secretary Dudas notes that the current allowance rate for business method patents is only about 11%. Graham, 71 Pat., Trademark & Copyright J. at 374.

The PTO has also put in place a second level of review. After the patent examiner allows an application, PTO supervisors test the allowed claims for patentability and thus exercise quality control. The patent allowance error rate

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[3] Figures 1 and 2 track the results of all patent applications from 1963 to 2004, including utility, design, and plant patents. But when utility patents only are examined (*i.e.*, the type of patent involved in this case), the numbers are even more telling. For example, in 2004, U.S.-based inventors filed 189,536 applications for utility patents. In that same year, only 84,271 patents were granted to U.S.-based applicants. That grant rate was only 44%. *See USPTO Patent Statistics*.

(*i.e.*, the percentage of allowed patents rejected after this second level of review) in 2005 was only about 4%, down from 5.32% in 2004. U.S. Pat. & Trademark Office, Proposed Rule Changes to Focus the Patent Process Involving Continuations, Double Patenting and Claims (Mar. 29, 2006), *at* http://www.uspto.gov/web/offices/pac/dapp/opla/presentation/connipla032906v1_text.html.

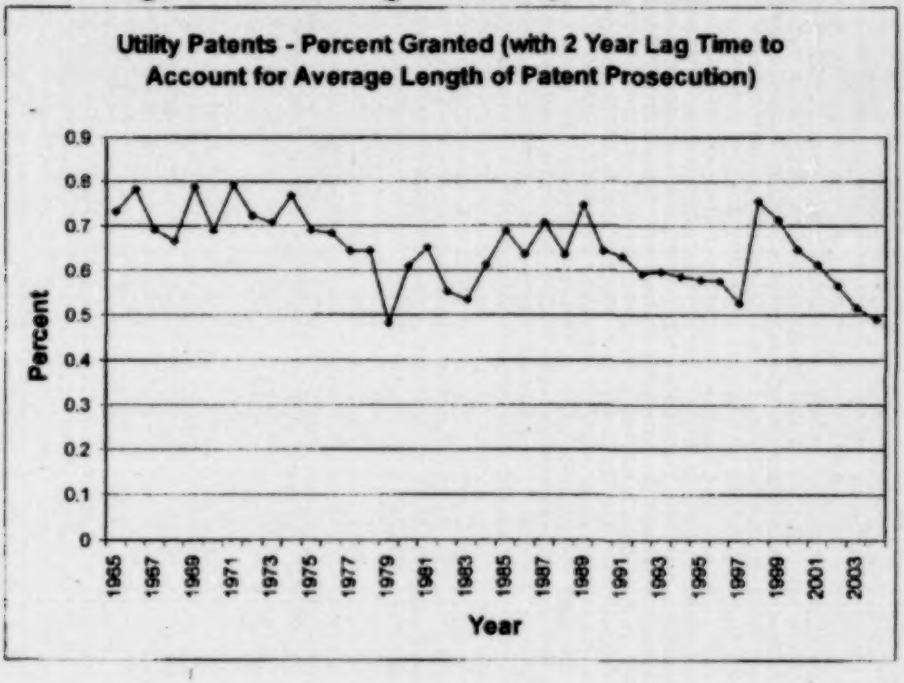
But that is not the end of PTO review. Patents can also be subjected to reexamination, either at the request of the patentee or, more often, an opponent. Indeed, in this case, MedImmune has requested reexamination of the Cabilly II patent (and thus does not even need to challenge the patent in court). In a reexamination, the requestor submits to the PTO prior art references and arguments against patentability that the PTO had not considered the first time. No presumption of validity applies. Even so, reexamination results in cancellation of the patent in only about 9.2% of the cases. That statistic alone confirms that the PTO generally did its job well the first time. In about 23% of the cases, the patent claims remain unscathed. In the rest of the cases, some claims are amended or some are cancelled but the patent as a whole survives. *See* Stuart J. Graham *et al.*, Post-Issue Patent "Quality Control": A Comparative Study of US Patent Re-examinations and European Patent Oppositions, 34 (2002), *available at* http://repositories.cdlib.org/iber/econ/E02-321 (analyzing all U.S. patents reexamined from 1980 to 1999).

As noted above, MedImmune claims that 74% to 98% of all applications are granted. *Brief for Petitioner* at 47. MedImmune derives these figures from a 2003 report by the Federal Trade Commission ("The FTC Report"). Fed. Trade Comm'n, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy* (2003). MedImmune fails to mention, however, that the FTC Report itself notes that there is a dispute over these figures and that,

for example, recent research has cast doubt on the 98% figure. *See id.* at ch. 5, 6 & nn.41–42; *see also* Robert A. Clarke, *U.S. Continuity Law and its Impact on the Comparative Patenting Rates of the US, Japan and the European Patent Office*, 85 J. Pat. & Trademark Off. Soc'y 335, 337–38 (2003) (noting that the 98% figure results from double counting errors).

The FTC Report proves only that the numbers can be deceiving. Thus, to test the BPLA's own calculations, the BPLA recalculated a subset of patents (utility patents, which is the category of patent involved in this case) and applied a two-year lag to account for the average length of patent prosecution. That is, an application filed in, say, 2002, will, on average, not be granted until 2004 or later. As seen in Figure 3 below, however, the trend is the same: the patent grant rate has steadily declined since the late 1990s, dipping to roughly 50% in recent years.

Figure 3. Percentage of Utility Patents Granted



As seen above, the PTO is continuing its trend of applying more scrutiny to utility patents. The result is that the allowance rate has been declining since before the Cabilly II patent issued.

MedImmune makes a similarly misleading argument about the success of patent validity challenges, claiming that 45% of patents are held invalid when validity is challenged and litigated to final judgment. *Brief for Petitioner* at 47 (*citing* FTC Report, ch. 5 at 6). But this figure, if accurate, proves nothing. Even the FTC Report itself warns that the figure should be "interpreted with caution . . . [because] self-selection in bringing and settling suits makes it unlikely that patents litigated to final results are fully representative of patents as a whole." *FTC Report*, ch. 5 at 6 n.38 (citing *Competition and Intellectual Property Law and Policy in the Knowledge-Based Economy: Hearing Before the Federal Trade Commission* at 92–93 (Jul. 10, 2002) (statement of Glynn S. Lunney, Jr.)); *see also* James Bessen & Michael J. Muerer, *Lessons for Patent Policy from Empirical Research on Patent Litigation*, 9 Lewis & Clark L. Rev. 1, 3–4 (2005) (patent suits "constitute a small and uncharacteristic subset" and that "selection bias distorts inferences based on statistics like patent holder win rates at trial"). In other words, disputes involving strong arguments for or against infringement and validity tend to resolve before trial, leaving only close cases for trial and appeal. One would expect a roughly 50% validity rate when such close cases go to final judgment. Thus, the 45% figure is unsurprising and meaningless.

### B. Any Solution, if One Is Needed, Should Come from Congress and the PTO

Granted, some patents escape effective scrutiny in the PTO and are defective. The BPLA does not claim that the system is perfect. But MedImmune's proposed solution — to allow

all licensees in good standing to challenge the licensed patents, whether those patents are valid or not — is too extreme and, ultimately, will discourage licensing. If there is a problem with patent quality, the solution should not be to upset the entire intellectual property system. Instead, Congress and the PTO should address the problem at its alleged source, whether by allocating appropriate funds to the PTO or otherwise by amending PTO rules to promote more effective patent scrutiny.

Prominent inventors like Dean Kamen prefer fixing any perceived problem at its source by improving the PTO's ability to examine patents. In recent testimony to the House Subcommittee on Courts, the Internet, and Intellectual Property, Mr. Kamen called for more funding to improve PTO examination of patents. In Mr. Kamen's opinion, "[w]ith state of the art search tools and access to the world's technical literature at their fingertips, along with proper training, supervision, and adequate time to do a quality job, many of the real and perceived problems with the patent system should fade away." *Patent Trolls: Fact or Fiction: Hearing Before the Subcomm. On Courts, the Internet, and Intellectual Property of the H. Comm on the Judiciary*, 109th Cong. 83 (2006) (statement of Dean Kamen, President, DEKA Research & Development Corp.) [hereafter *Kamen Congressional Testimony*].[4]

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[4] Mr. Kamen, a member of the National Inventors Hall of Fame and recipient of the Heinz Award in Technology, among other honors, holds more than 150 U.S. and foreign patents, including patents directed to life-saving technologies like infusion pumps for neonates, wearable insulin pumps for diabetics, kidney dialysis machines for home use, and heart stents. Mr. Kamen's company, DEKA Research & Development Corporation, licenses many of these patents to medical device companies, who manufacture and market these life-saving products. *Kamen Congressional Testimony, supra*, at 1.

Under Secretary Dudas reports that many PTO initiatives to improve and streamline patent examination have already borne fruit and have improved patent quality, for example, by lowering the allowance error rate. Indeed, as seen above, when the PTO hired and trained additional examiners and implemented changes in the way it reviews applications for business method patents, quality improved dramatically. More initiatives, such as the hiring of additional examiners, are underway. Graham, *Perception Gap*, *supra*, at 374. Thus, experience shows that increased funding and legislation will actually pay dividends.

As argued in Section II below, rewriting jurisdiction rules to allow licensees in good standing to sue will upset the balance between licensors and licensees, between intellectual property creators and users. In particular, allowing licensees in good standing to sue will undermine the confidence that innovators and investors have in licensed patents. Any rule that undermines faith in intellectual property will be, in the words of Mr. Kamen, like "flood[ing] the building to put out a fire in a wastepaper basket." *Kamen Congressional Testimony*, *supra*, at 83.

## II. ALLOWING LICENSEES IN GOOD STANDING TO SUE WILL UNDERMINE LICENSES AND HARM THE ECONOMY

MedImmune was pleased to take a license from Genentech when it sold no products covered by a licensed patent and thus paid no royalties. The license cost MedImmune almost nothing. MedImmune benefited from that *de facto* royalty-free license for a number of years, during which time MedImmune enjoyed peace (for free) from litigation. As MedImmune concedes, when it agreed to the license, it "was a new company unable to afford extended litigation and unwilling to risk crippling infringement judgments . . . ." *Petition for a Writ of Certiorari* ("Petition") at 3.

After taking the license, MedImmune began to market a commercially successful product, Synagis®, which, according to MedImmune, accounts for 80% of its profits. *See* Petition at 4. Back in 1997, however, when MedImmune negotiated the license, MedImmune obtained a low royalty rate because, at the time, it had not yet gained FDA approval to sell Synagis® and thus lacked any track record of commercial success (which is often a factor in determining a royalty rate). *See Brief of Respondent Genentech, Inc.*, at 5–8 ("The resulting license terms reflected these advantagesous bargaining conditions. The upfront payment was modest, and the royalty rate was heavily discounted").

But after Synagis® became profitable and as soon as MedImmune learned it would have to pay royalties—which would cut into MedImmune's substantial profits from the drug—MedImmune sought to challenge the Cabilly II patent while preserving its low royalty rate. Indeed, MedImmune apparently admits that the increasing profitability of the product was the impetus for this lawsuit: "With demand for Synagis® growing, and payments to Genentech correspondingly rising, on April 11, 2003, MedImmune brought suit . . ." *Brief for Petitioner* at 7.

MedImmune, it seems, has a history of ducking inconvenient infringement litigation (*e.g.*, before Synagis® became profitable and the stakes were low) by taking a license and then challenging the underlying patent when it becomes expedient to do so (*e.g.*, after Synagis® became profitable and the stakes became high). *See MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376, 1377-78 (Fed. Cir. 2005) (describing behavior similar to MedImmune's in this case and affirming dismissal for lack of an actual controversy).

MedImmune cannot complain that it was somehow tricked. When MedImmune signed up for the license, it knew that the

license covered a number of pending patent applications, including the application that eventually matured into the so-called "Cabilly II patent." *Petition for Writ of Certiorari* at 3. ("The license package also included . . . several patent applications that were pending, among them what became the Cabilly II patent . . .").

This calculating behavior does not justify departing from the Article III actual controversy standard. Allowing MedImmune to maintain its declaratory judgment action will have the unintended and harmful result of undermining faith in intellectual property licenses. But public policy encourages licensing and settlement of patent disputes, even if some allegedly invalid patents are left unchallenged.

### A. The U.S. Benefits From Licenses

The United States benefits enormously from the licensing of patented technologies. Thus, a judicial or legislative body should exercise extreme caution before tampering with the current and long-existing balance between and expectations of licensors and licensees.

Institutions responding to an Association of University Technology Managers survey in 2004 reported that 137 entities had introduced 567 new commercial products to the marketplace under license agreements with commercial partners. *See* Assoc. of University Tech. Managers, *AUTM U.S. Licensing Survey: FY 2004: A Survey Summary of Technology Licensing (and Related) Performance for U.S. Academic and Nonprofit Institutions, and Technology Investment Firms* 2 (Ashley J. Stevens et al. eds., 2005) *available at* http://www.autm.net/events/File/FY04%20Licensing%20Survey/04AUTM-USLicSrvy-public.pdf.

In the same year, licensing income totaled $1.385 billion spread out among 196 institutions. *Id.* at 3. Some of the

new products resulting from U.S. licensing activities included improved blood glucose monitoring devices for diabetics, an experimental vaccine to combat parasitic infections, and a chemical decontaminant capable of destroying chemical warfare agents. *Id.* at 3–9. Educational and non-profit institutions benefit from licensing by gaining revenue sources to help pay for further research. Indeed, in 2000 alone, universities realized over $1 billion from licensing and capitalizing intellectual property. Bessen & Muerer, *supra*, at 13.

Well-known institutions like Harvard University, the Dana-Farber Cancer Institute, and St. Jude Children's Research Hospital frequently obtain patents and license their discoveries to others. *See* Assoc. of University Tech. Managers, *supra*, at 31–32

Manufacturers also benefit from being able to make and sell new products that the inventors had no interest in making or could not have made themselves. Indeed, even traditional and Rust Belt manufacturers like John Deere recognize that "the ability to keep inventing new products that are useful to customers is still the key to Deere's growth." Carol Hymowitz, *For Now, the Focus Is More on Innovation than on Budget Cuts*, Wall St. J., July 17, 2006, at B1. Deere, however, recognizes that it would be too costly to do all of its research and development in-house, which would mean hiring more engineers and competing for talent with high-tech companies, thus driving up costs. Instead, "[t]o stretch research dollars, Deere works with universities and small companies" to augment its development of innovative products. *Id.*

In other words, universities and small businesses can profit from licensing their discoveries to large manufacturers, who in turn profit by reducing the costs of innovation. That's the idea behind Mr. Kamen's success. As Mr. Kamen told the

House Subcommittee, his business model is to invent, not to manufacture, market, and sell. Thus, he licenses his patented technologies to companies that are better able to bring Kamen's life-saving technologies to market. In turn, the companies get exclusive patent protection without having to spend as much as they otherwise would on research and development. *Kamen Congressional Testimony*, *supra*, at 20–22.

Large companies also license their own discoveries to others, not only to make money but also to commercialize their discoveries more widely. For example, IBM earned $367 million in 2005 alone from licensing. IBM, *2005 Annual Report* 26 (2006), *available at* ftp.software.ibm.com/annualreport/2005/2005_ibm_annual.pdf. Hewlett-Packard gains roughly $200 million "worth of value from its intellectual property" annually, which includes royalty payments to the company and discounts on royalty payments to other companies that it would otherwise have to pay. Michael Kanellos, *HP Plays the Patent Game*, CNET News.com, Nov. 10, 2005, *at* http://news.com.com/HP+plays+the+patent+game/2100-1008_3-5944056.html.

In the biotech and pharmaceutical industries (those implicated in this case), the licensing of patents has led to enormous benefits for the health of the American people. For instance, Taxol, a potent cancer-fighting drug, was the result of Florida State University Professor Robert Holton's 1991 invention of a way to synthesize paclitaxel, the active compound in Taxol, using the compounds found in the needles and twigs of the common English Yew tree. Holton's invention allowed Taxol to be mass produced more economically. The Assoc. of University Tech. Managers, *Technology Transfer Stories: 25 Innovations That Changed the World*, 103 (2006), *available at* http://www.autm.net/documents/AUTM_BWR.pdf. Holton eventually licensed his invention to Bristol-Myers Squibb, which introduced the

drug to the marketplace in 1993 and has since been used by more than two million women worldwide. *Id.* at 103–04. Without Holton's invention and the license agreement with Bristol-Myers Squibb, a potent cancer fighting drug would not have been available to millions of women.

Another invention that has saved lives is Exosurf, a synthetic surfactant for use in the lungs that has dramatically cut the death rate of premature infants suffering from respiratory distress syndrome (RDS). *Id.* at 51–54. In 1986, the inventor, John Clements, a university professor and researcher, licensed Exosurf to Burroughs-Wellcome (now GlaxoSmithKline), which brought the drug to market. Since then, use of the drug has dramatically cut infant mortality from RDS. *Id.* Without licensing, this product would have taken much longer to reach the market, and more premature newborns would have died.

### B. Public Policy Encourages Upholding the Integrity of Licenses Even if Some Invalid Patents Remain Unchallenged

Allowing a licensee in good standing to challenge the validity of a patent while maintaining the benefits of the license (such as a locked-in, low royalty rate) will disrupt licensing activities and harm the economy. Doing so will make licensing more costly and make patent owners hesitant to license their inventions. If patent owners cannot count on settling disputes through licenses, and if inventors cannot count on their licensees to abide by the patents, then investors and businesses will have less incentive to support research and development and promote the introduction of new technologies. Indeed, common sense dictates that a patent owner will be wary of handing out a license knowing that the recipient will eventually bite the proverbial hand. Such loss of faith in the value of licenses could ultimately

reduce the commercialization of innovative products like the ones recounted above.

Predictability in the patent system is crucial to promoting the costs and risks associated with innovation. In turn, innovation is at the heart of American competitiveness in the global economy. David Silverstein, *Patents, Science and Innovation: Historical Linkages and Implications for Global Technological Competitiveness*, 17 Rutgers Computer & Tech. L.J. 261, 318–19 (1991); *see also Hilton Davis Chem. Co. v. Warner-Jenkinson Co. Inc.*, 62 F.3d 1512, 1529 (Fed. Cir. 1995) ("Technologic innovation has driven the American economy, over the past century, to the exclusion of virtually all other growth factors") (Newman, J, dissenting), *rev'd*, 520 U.S. 17 (1997); Reed Albergotti, *The Most Inventive Towns in America*, Wall St. J., July 22, 2006, at P6 ("One upside of these innovations is that new patents often lead to the creation of new companies, which in turn means more jobs")

Allowing licensees in good standing to maintain declaratory judgment actions while retaining the benefits of their licenses, however, will disrupt the predictability of license agreements and "effectively defeat those contractual covenants and discourage patentees from granting licenses." *Gen-Probe Inc. v. Vysis, Inc.*, 359 F.3d 1376, 1382 (Fed. Cir. 2004). In other words, the public will lose faith in licenses.

In this case, MedImmune admits that it accepted a license in 1997 to avoid litigation, to settle a dispute. But public policy encourages preserving the integrity of licenses and promoting settlement of actual or threatened litigation, even if some invalid patents remain unchallenged. *See, e.g., Flex-Foot, Inc. v. CRP, Inc.*, 238 F.3d 1362, 1368 (Fed. Cir. 2001) ("[W]hile the federal patent laws favor full and free competition in the use of ideas in the public domain over the technical requirements of contract doctrine, settlement of

litigation is more strongly favored by the law"); *accord, In re Tamoxifen Citrate Antitrust Litigation*, 429 F.3d 370, 386-87 (2d Cir. 2005) (citing *Flex-Foot* and observing that rules discouraging settlements of patent litigation "would heighten the uncertainty surrounding patents and might delay innovation"); *see also Schering-Plough Corp. v. Federal Trade Comm'n*, 402 F.3d 1056, 1072 (11th Cir. 2005) ("The general policy of the law is to favor the settlement of litigation, and the policy extends to the settlement of patent infringement suits"); *Hemstreet v. Spiegel, Inc.*, 851 F.2d 348, 351 (Fed. Cir. 1988) (holding that *Lear v. Adkins*, 395 U.S. 653 (1969), did not preclude the enforcement of a settlement even if the licensed patents may be held invalid or unenforceable); *Wells Cargo, Inc. v. Wells Cargo, Inc.* 606 F.2d 961, 965 (C.C.P.A. 1979) ("If there be a policy favoring challenges to trademark validity, it too has been viewed as outweighed by the policy favoring settlements").

This Court itself recognizes that the exchange of rights and royalties to settle patent litigation "may promote rather than restrain competition." *Standard Oil Co. v. United States*, 283 U.S. 163, 171 (1931).

The notion that only invalid patents are likely to be challenged is dubious. Licensees have a strong incentive to challenge patents — no matter whether the case for invalidity is strong or weak — so that they can avoid paying additional royalties. Allowing licensees in good standing to sue will thus skew the balance between licensor and licensee. *See Gen-Probe*, 359 F.3d at 1382 ("[T]he licensor would bear all the risk, while the licensee would benefit from the license's effective cap on damages or royalties in the event its challenge to the patent's scope or validity fails"). Of course, litigation will increase as well.

Even if only invalid patents are challenged, there is no guarantee that the public will reap the benefits. As Circuit

Judge Newman of the Federal Circuit noted, validity challenges do not always benefit the public:

> The Court in *Lear* apparently believed that "full and free competition" ensues when a patent is eliminated from the rolls. The experience of the marketplace is otherwise. The usual incentive to the patent licensee in taking the license is, and always has been, the opportunity for profit. If the destruction of a licensed patent would not enhance profits but instead facilitate the entry of competitors, this would surely be weighed by a licensee before embarking on a *Lear*-authorized challenge to the licensed patent. It is common experience — and common sense — that challenges to patent validity by either licensees or assignors, albeit serving the private interest of the challenger, carry scant public benefit. The nobler expectations of *Lear* have few testimonials.

*Diamond Scientific Co. v. Ambico, Inc.*, 848 F.2d 1220, 1228 (Fed. Cir. 1988) (Newman, J., concurring) (citation omitted).

Rather than pass the benefit of reduced costs on to the public, the unfortunate truth is that licensees like MedImmune will keep for themselves the money they would have paid in royalties and thus enjoy higher profits. Armed with the ability to challenge the validity of patents while protected by license agreements, licensees will have a strong incentive to risk litigation to challenge even valid patents.

Altering the rights of patentees and licensees as MedImmune suggests is not an experiment to undertake lightly. Licensing is too important to the American economy and well-being of the American people to change the expectations of patentees

and licensees simply because one licensee, MedImmune, wants to keep more of its profits for itself. If any such changes in expectations are to occur, they should be the result of open and careful deliberation in Congress, based on the input of many intellectual property creators and users.

## CONCLUSION

The Boston Patent Law Association urges this Court to affirm the ruling of the Federal Circuit that a licensee in good standing — who, by definition, has not apprehension of suit — may not create declaratory judgment jurisdiction under Article III merely because it desires to challenge the validity of the licensed patent.

Respectfully Submitted

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IN THE

# Supreme Court of the United States

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MEDIMMUNE, INC.,

*Petitioner*,

v.

GENENTECH, INC., *et al.*,

*Respondents*.

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**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

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## BRIEF *AMICUS CURIAE* OF THE GENERIC PHARMACEUTICAL ASSOCIATION IN SUPPORT OF PETITIONER

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## BRIEF *AMICUS CURIAE* OF THE GENERIC PHARMACEUTICAL ASSOCIATION IN SUPPORT OF PETITIONER

## INTEREST OF *AMICUS CURIAE* [1]

*Amicus curiae* Generic Pharmaceutical Association ("GPhA") represents over 120 companies that manufacture more than ninety percent of all affordable prescriptions dispensed in the United States each year, accounting for more than one billion prescriptions annually.

[1] Letters evidencing the parties' consent to the submission of this brief have been lodged with the Clerk. Pursuant to this Court's Rule 37.6, *amicus* states that no counsel to a party authored this brief in whole or in part and no person other than *amicus* and its members made a financial contribution towards the preparation and submission of the brief.

Generic drug companies have a vital interest in this case because the ability of generic drug companies to bring declaratory judgment actions against holders of pharmaceutical patents is critical to their ability to bring less expensive generic pharmaceuticals to market quickly. Congress explicitly authorized such declaratory judgment actions when it amended the Hatch-Waxman Act in 2003 to permit generic companies to bring a civil action "to obtain patent certainty." 21 U.S.C. § 355(j)(5)(C).

The reasoning applied by the Federal Circuit in this and other cases has effectively prevented generic drug companies from pursuing declaratory judgment actions even in situations in which Congress has expressly authorized them. In *Teva Pharmaceuticals USA, Inc. v. Pfizer, Inc.*, 395 F.3d 1324, 1333, *reh'g en banc denied*, 405 F.3d 990 (Fed. Cir.), *cert. denied*, 126 S. Ct. 473 (2005) ("*Teva v. Pfizer*"), the Federal Circuit upheld the dismissal of a declaratory judgment action brought by a generic drug company, ruling that Article III precluded subject matter jurisdiction unless the plaintiff demonstrates that it faces a "reasonable apprehension of imminent suit" by the patentee. In this case, the Federal Circuit applied the same "reasonable apprehension" test to preclude petitioner's declaratory judgment action. In both cases, and in many other patent declaratory judgment actions, a justiciable controversy was unquestionably presented under this Court's Article III jurisprudence.

GPhA has been permitted to submit *amicus* briefs in both the Federal Circuit and in this Court to urge the recognition that declaratory judgment actions by generic companies are essential components of the country's efforts to moderate the ever-increasing costs of prescription drugs and fall comfortably within this Court's standards of justiciability under

Article III.[2] GPhA submits this brief to stress the untoward impact that the "reasonable apprehension" requirement has on a wide range of cases that do not involve the licensing of patents and its inconsistency with Article III, the Declaratory Judgment Act, and the patent laws.

## SUMMARY OF ARGUMENT

The Federal Circuit erred in ruling that MedImmune had failed to demonstrate the existence of a justiciable "actual controversy," as required by Article III and the Declaratory Judgment Act, because MedImmune faced no "reasonable apprehension" of a patent infringement suit by Genentech. *MedImmune, Inc. v. Genentech, Inc.*, 427 F.3d 958, 964-65 (Fed. Cir. 2005), *cert. granted*, 126 S. Ct. 1329 (2006). The court of appeals erred because its "reasonable apprehension of suit" requirement undermines one of the principal purposes of the Declaratory Judgment Act and finds no support in this Court's Article III jurisprudence.

The Declaratory Judgment Act was enacted to provide a mechanism for a party to obtain definitive judicial resolution of legal claims where claimants *refuse* to bring suit. Congress sought to relieve a prospective defendant of the Hobson's Choice between incurring mounting potential liability and foregoing legitimate business or other opportunities. The Federal Circuit's insistence that the declaratory judgment plaintiff reasonably apprehend the imminent commencement of litigation before seeking relief from such a dilemma effectively eliminates the possibility of relief in the situations in which Congress intended such relief to be available.

---

[2] GPhA submitted *amicus* briefs in this Court in support of the certiorari petitions in *Teva Pharmaceuticals USA, Inc. v. Pfizer, Inc.*, No. 05-48 (*cert. denied* on Oct. 11, 2005) and *Apotex, Inc. v. Pfizer, Inc.*, No. 05-1006 (*petition for certiorari filed* Feb. 9, 2006). It submitted *amicus* briefs in the Federal Circuit in *Teva v. Pfizer*.

The reasonable apprehension of suit requirement is inconsistent with this Court's Article III decisions. The only Article III requirement for declaratory judgment actions is that the dispute sought to be resolved be "definite and concrete, touching the legal relations of parties having adverse legal interests," "admitting of specific relief through a decree of a conclusive character, as distinguished from an opinion advising what the law would be upon a hypothetical state of facts." *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 241 (1937).

The Article III requirements are met in this case. The constitutional standard is also met in declaratory judgment actions brought by generic drug companies pursuant to the 2003 amendments to the Hatch-Waxman Act that authorized generic companies to bring a "civil action to obtain patent certainty," 21 U.S.C. § 355(j)(5)(C)(i)(II), and directed district courts to exercise subject matter jurisdiction over such claims "to the extent consistent with the Constitution," 35 U.S.C. § 271(e)(5). However, the Federal Circuit's application of the "reasonable apprehension" test has effectively reduced these amendments to a dead letter by precluding any successful prosecution of such actions.

The Federal Circuit's application of the "reasonable apprehension" test in this case is not saved because the patent licensor is unable to bring suit against the licensee until the licensee breaches the license. This Court has permitted declaratory judgment actions to proceed even where the underlying claim of the declaratory judgment defendant against the declaratory judgment plaintiff has not accrued. The Federal Circuit's reliance on what it referred to as "equalizing principles" is therefore misplaced.

Because MedImmune asserted an "actual controversy," the Federal Circuit's decision should be reversed.

## ARGUMENT

### I. CONGRESS INTENDED TO PERMIT PARTIES TO SEEK RESOLUTION OF PATENT DISPUTES WHERE PATENTEES DECLINE TO BRING INFRINGEMENT ACTIONS.

#### A. The Declaratory Judgment Act.

The Declaratory Judgment Act was enacted in 1934 in large part to permit parties to obtain definitive judicial determinations of non-infringement and invalidity in patent disputes in which the patentee chooses *not* to initiate patent infringement litigation. As Congress recognized, before the Declaratory Judgment Act such parties faced a Hobson's Choice between commencing (or continuing) potentially infringing conduct (and thereby risking often ruinous liability) or foregoing legitimate business opportunities (if the parties or their customers found the risks of liability unacceptably high).[3] The Declaratory Judgment Act was intended to provide a mechanism for parties to avoid that dilemma by obtaining a definitive judicial resolution *before* commencing or continuing potentially infringing conduct.

In *Cardinal Chemical Co. v. Morton International, Inc.*, 508 U.S. 83, 95-96 (1993), this Court underscored the importance of declaratory judgment actions in resolving

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[3] *See* S. Rep. No. 73-1005, at 2 (1934) (citing declaratory judgment action's utility in "avoiding the necessity, now so often present, of having to act at one's peril or to act on one's own interpretation of his rights, or abandon one's rights because of a fear of incurring damages"); Hearings Before a Subcomm. of the S. Comm. on the Judiciary on H.R. 5623, 70th Cong. 35 (1928) (statement of E.R. Sunderland) (citing Hobson's Choice faced by manufacturers of potentially patented devices); Hearing Before the H. Comm. on the Judiciary on H.R. 5030, H.R. 10141, H.R. 10142, and H.R. 10143, 67th Cong. 10 (1922) (statement of Henry W. Taft, American Bar Association) (noting utility of declaratory judgment actions in patent disputes).

patent disputes in which the patentee is *not* about to bring suit. This Court referred to

> the sad and saddening scenario that led to enactment of the Declaratory Judgment Act (Act), 28 U.S.C. § 2201. In the patent version of that scenario, a patent owner engages in a *danse macabre*, brandishing a Damoclean threat with a sheathed sword . . . . Before the Act, competitors victimized by that tactic were rendered helpless and immobile so long as the patent owner refused to grasp the nettle and sue. After the Act, those competitors were no longer restricted to an *in terrorem* choice between the incurrence of a growing potential liability for patent infringement and abandonment of their enterprises; they could clear the air by suing for a judgment that would settle the conflict of interests. The sole requirement for jurisdiction under the Act is that the conflict be real and immediate, i.e., that there be a true, actual "controversy" required by the Act.

*Id.* at 95-96 (quoting *Arrowhead Indus. Water, Inc. v. Ecolochem, Inc.*, 846 F.2d 731, 734-35 (Fed. Cir. 1988)). This Court went on to note that the desire of a company to "avoid the threat of a 'scarecrow' patent . . . may therefore be sufficient to establish jurisdiction under the Declaratory Judgment Act." *Id.* at 96.

The phrase "scarecrow patent" derives from Judge Learned Hand's opinion in *Bresnick v. United States Vitamin Corp.*, 139 F.2d 239 (2d Cir. 1943). In that case, although the patentee sued the defendant only on one claim of its patent, the court ruled that the patent in its entirety was invalid. Judge Hand observed, "[w]e have disposed of the patent as a whole because it has seemed to us proper that it should not remain in the art as a scarecrow." *Id.* at 242. A scarecrow patent is one that is *not* asserted by the patentee in an infringement action, but nevertheless serves to "scare off" potential customers of the patentee's competitors. The point of this Court's reference to "scarecrow patents" in *Cardinal*

*Chemical* was that the Declaratory Judgment Act was meant to provide a means to eliminate the competitive barriers caused by such patents by allowing potential infringers to obtain "patent certainty" even where there is no infringement claim asserted.[4]

### B. The Hatch-Waxman Act And Its 2003 Amendments.

Congress confirmed the important role of declaratory judgment actions in offering "patent certainty" to parties faced with the "*in terrorem* choice" to which this Court referred in *Cardinal Chemical* when it amended the Hatch-Waxman Act in 2003 to create a "civil action to obtain patent certainty" for a generic drug company that files an Abbreviated New Drug Application ("ANDA"). 21 U.S.C. § 355(j)(5)(C).

As enacted in 1984, the Hatch-Waxman Act gave the holder of a pharmaceutical patent the right to sue an ANDA applicant immediately for patent infringement if the ANDA applicant sought FDA approval to launch a generic formulation of the pioneer drug before the expiration of the patent. 35 U.S.C. § 271(e)(2)-(4); *see Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 675-78 (1990). Congress created this statutory act of infringement to permit the resolution of patent disputes before the expiration of potentially blocking patents and thereby to accelerate the introduction of less expensive generic drugs. *Eli Lilly*, 496 U.S. at 676-78.

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[4] *Accord Clair v. Kastar, Inc.*, 148 F.2d 644, 646 (2d Cir. 1945) (L. Hand, J.). In *Clair*, the court stressed that the Declaratory Judgment Act provides a remedy to potential infringers that believe themselves to be harmed by a patentee's delay in asserting an infringement claim:

> [I]f a manufacturer fears that he will be charged to infringe, he can always inquire of the patentee, and if the answer is unsatisfactory, he can bring an action for a declaratory judgment. *The time has now passed when a patentee may sit by and refuse to show his hand.*

*Id.* (emphasis added).

By 2003, however, Congress recognized that some drug companies had sought to "delay infringement litigation between generic drug manufacturers and pioneer drug companies." H.R. Conf. Rep. No. 108-391, at 836 (2003), and thereby deny the public the benefit of less costly generic drugs, *see Eli Lilly*, 496 U.S. at 676. In response, Congress expressly extended to ANDA applicants the same opportunity to initiate early judicial resolution of patent disputes that the original Hatch-Waxman Act gave to patentees. The 2003 legislation authorized ANDA applicants to bring a "civil action to obtain patent certainty" for a declaration of patent invalidity or non-infringement, if the patentee had not commenced an infringement action within 45 days of the infringing ANDA filing. 21 U.S.C. § 355(j)(5)(C)(i)(II); 35 U.S.C. § 271(e)(5).

This statutory leveling of the playing field never had a chance to work. In *Teva Pharmaceuticals USA, Inc. v. Pfizer, Inc.*, 395 F.3d 1324, 1333, *reh'g en banc denied*, 405 F.3d 990 (Fed. Cir.), *cert. denied*, 126 S. Ct. 473 (2005) ("*Teva v. Pfizer*"), the first case to reach the Federal Circuit under the new law, the court of appeals ruled that Article III itself requires that an ANDA applicant suing to obtain patent certainty prove that it faces a "reasonable apprehension of imminent suit" by the patentee, a situation that will almost never exist when there has been no action commenced within 45 days of the ANDA filing. The Federal Circuit thus precluded "civil action[s] to obtain patent certainty" in the only situations in which they were intended to be available. In effect, the court of appeals ruled that the Constitution precluded Congress from leveling the playing field.[5]

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[5] The *Teva v. Pfizer* majority expressed the view that its holding was consistent with Congress' intent, 395 F.3d at 1336, but this view makes no sense. Initially, it was pure dictum because if, as the court held, Article III requires a "reasonable apprehension of imminent suit," then it obviously does not matter what Congress intended to do. Beyond that, the upshot of

This effective nullification of the statutory "civil action to obtain patent certainty" will result in delays in introducing many generic drugs, delays that will have a significant, negative impact on the nation's health care system. Data published by the federal Centers for Medicare & Medicaid Services indicate that national expenditures for prescription drugs have risen from $12 billion in 1980 to $188.5 billion in 2004.[6] Generic drugs play a critical role in moderating this explosive growth in the cost of prescription drugs. A study published by the Federal Trade Commission in 2002 reported that average drug prices declined 20 percent within two years of generic drug entry into the market and that the savings increase with the number of generic competitors.[7]

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the *Teva v. Pfizer* court's reasoning was that, by creating a new "civil action to obtain patent certainty," Congress intended to permit declaratory judgment actions in precisely the same circumstances in which they were permitted under Federal Circuit precedent before the legislation was passed. Congress does not usually enact legislation in order to preserve the legal status quo.

The conference committee report cited by the court of appeals, *id.* at 1336-37, shows that the conferees expected the courts to apply the reasonable apprehension test if, but only if, the Constitution required it, but expressed no views on whether the constitution required it, a decision reserved for the judicial branch. Such an expectation reflected the command set forth in the legislation that district courts exercise jurisdiction over declaratory judgment actions brought by ANDA applicants "to the extent consistent with the Constitution." 35 U.S.C. § 271(e)(5).

[6] These data can be found at http://www.cms.hhs.gov/NationalHealthExpendData/downloads/tables.pdf.

[7] Federal Trade Commission Generic Drug Entry Prior to Patent Expiration: An FTC Study 9 (2002), *available at* http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf.

## II. THE FEDERAL CIRCUIT'S "REASONABLE APPREHENSION OF SUIT" REQUIREMENT IS INCONSISTENT WITH THE COURT'S ARTICLE III JURISPRUDENCE.

### A. The Constitution And The Declaratory Judgment Act Require An "Actual Controversy".

The "actual controversy" requirement in the Declaratory Judgment Act "manifestly has regard to [Article III] and is operative only in respect to controversies which are such in the constitutional sense." *Aetna*, 300 U.S. at 239-40. As this Court stated in *Aetna*, a claim for declaratory relief is justiciable if it is "definite and concrete, touching the legal relations of parties having adverse legal interests," "admitting of specific relief through a decree of a conclusive character, as distinguished from an opinion advising what the law would be upon a hypothetical state of facts." *Id.* at 240-41.

This Court later crystallized this "irreducible constitutional minimum" in terms of the now familiar requirements of injury in fact, traceable to the conduct of the defendant and redressable by the requested relief. *Bennett v. Spear*, 520 U.S. 154, 162 (1997). *Accord Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 102-03 (1998). *See Duke Power Co. v. Carolina Envtl. Study Group, Inc.*, 438 U.S. 59, 79 (1978) ("We ... cannot accept the contention that ... a litigant must demonstrate something more than injury in fact and a substantial likelihood that the judicial relief requested will prevent or redress the claimed injury to satisfy the 'case or controversy' requirement of Article III."). Although the Court in *Bennett* and *Steel Co.* articulated this standard as a "standing" requirement, it serves as the irreducible minimum requirement of Article III for related justiciability doctrines such as ripeness. *See Duke Power*, 438 U.S. at 81.

### B. The Federal Circuit's Two-Part Test For Jurisdiction In Declaratory Judgment Actions Requires More Than An "Actual Controversy".

In cases in which a declaratory judgment plaintiff seeks a declaration that a patent is invalid or not infringed by the product that the plaintiff proposes to sell, the Federal Circuit has formulated its own two-part test ostensibly to implement the requirements of Article III.

#### 1. *This case presents no issue concerning the first element of the Federal Circuit's jurisdictional test.*

The first element of the Federal Circuit's test is that the declaratory judgment plaintiff have engaged in "activity . . . which could constitute infringement, or concrete steps taken with the intent to conduct such activity." *Teva v. Pfizer*, 395 F.3d at 1332 (citing *Gen-Probe Inc. v. Vysis, Inc.*, 359 F.3d 1376, 1380 (Fed. Cir.), *cert. dismissed*, 543 U.S. 941 (2004)).

Although in this case the Federal Circuit did not discuss this first part of its test for an "actual controversy," MedImmune plainly satisfied it. It was marketing a specific drug, Synagis®, that Genentech claimed was within the scope of its patents. Moreover, whether Synagis® does in fact infringe those patents (or would infringe absent a license) and whether Genentech's patents are valid are "definite and concrete" questions that "touch[] the legal relations of parties having adverse legal interests," and "admit[] of specific relief through a decree of a conclusive character," *i.e.*, a declaration that specific patents are or are not valid and that a specific product (Synagis®) does or does not infringe them. MedImmune is clearly eager to sell its product immediately without paying royalties. Genentech is just as clearly unwilling to permit it to do so. MedImmune is paying royalties "under protest," and its declaratory judgment action seeks to "lift the

heavy hand of that tribute." *Altvater v. Freeman*, 319 U.S. 359, 365 (1943).

### 2. *The second element of the Federal Circuit's jurisdictional test is required neither by Article III nor by the Declaratory Judgment Act.*

The second requirement of the Federal Circuit's test for an actual controversy is "an explicit threat or other action by the patentee which creates a reasonable apprehension on the part of the declaratory judgment plaintiff that it will face an infringement suit," *Teva v. Pfizer*, 395 F.3d at 1332. The Federal Circuit requires that the infringement suit be "imminent." *Id.* at 1333. The Federal Circuit found MedImmune unable to satisfy this requirement because it remained in compliance with its license from Genentech, albeit under protest, and therefore faced no apprehension of suit. *MedImmune*, 427 F.3d at 964-65.

MedImmune argues to this Court that, whatever the merits of requiring a reasonable apprehension of imminent litigation in general, it should not bar a declaratory judgment action brought by a licensee simply because the licensee remains in compliance with the terms of the license. According to MedImmune, the Federal Circuit's categorical requirement that a licensee stop paying royalties before seeking a declaration of invalidity or non-infringement goes too far where, as here, the Article III requirements of an actual controversy genuinely admitting of specific relief by a decree of a conclusive character were satisfied.

MedImmune's arguments are correct as far as they go, but they do not go far enough. The "reasonable apprehension of imminent suit" requirement *itself* constitutes an unwarranted limitation on the jurisdiction of every district court in the United States in patent cases. It prevents the resolution of disputes that satisfy the requirements of Article III and

thwarts the purposes of both the Declaratory Judgment Act itself and the recent Hatch-Waxman Act amendments.

### C. Article III Controversies Often Arise Even When The Patentee Is Not About To Commence An Infringement Action.

There are many circumstances in which a patentee will not be on the verge of commencing patent infringement litigation despite the occurrence of arguably infringing conduct or the existence of other facts that create a justiciable Article III controversy. A principal purpose of the Declaratory Judgment Act is to provide a procedural mechanism for the declaratory judgment plaintiff to obtain a binding judicial resolution of a dispute in precisely those circumstances. This Court recognized this in *Cardinal Chemical*, 508 U.S. at 95-96.

For example, courts have recognized that patentees who face numerous infringers may sue sequentially rather than undertake multiple infringement actions simultaneously. The legitimacy of a patentee's pursuing its infringement claims seriatim has served to defeat the defense of laches to a delayed infringement claim. *See, e.g., Hemstreet v. Computer Entry Sys. Corp.*, 972 F.2d 1290, 1293 (Fed. Cir. 1992); *Vaupel Textilmaschinen KG v. Meccanica Euro Italia S.P.A.*, 944 F.2d 870, 876-77 (Fed. Cir. 1991); *Clair v. Kastar, Inc.*, 148 F.2d 644, 646 (2d Cir. 1945). Significantly, many of these cases have noted that an alleged infringer can avoid any prejudice from such delay by bringing a declaratory judgment action, which is assumed to be available even though the alleged infringer cannot reasonably apprehend imminent infringement litigation. 6 CHISUM ON PATENTS §19.05[2][d], at 19-641 & n.204 (2006) (citing cases).

A further example of particular concern to *amicus curiae* arises in the generic drug approval process set forth in the Hatch-Waxman Act. Developers of new drugs must list in an

FDA publication (commonly referred to as the "Orange Book") all patents that could "reasonably" be asserted against generic formulations of the drugs. 21 U.S.C. § 355(b)(1)(G), (c)(2). *See Teva v. Pfizer*, 395 F.3d at 1328. If a generic drug company files an ANDA with respect to such a drug, it must certify as to every Orange Book patent for that drug whether the generic company seeks to launch before the expiration of such patent on the ground that the patent is invalid or would not be infringed by its generic formulation. As noted above, that certification constitutes an "act of infringement" sufficient to trigger jurisdiction over a patent infringement suit by the patentee. 35 U.S.C. § 271(e); *Eli Lilly*, 496 U.S. at 678. If the patentee commences litigation within 45 days of the ANDA applicant's certification, then FDA approval of the ANDA is automatically stayed for 30 months. 21 U.S.C. § 355(j)(5)(B)(iii).

While the prospect of a 30-month stay of FDA approval is often sufficient incentive to the patentee to bring suit, there are many circumstances in which it is in the interests of the patentee to lie low. *Teva v. Pfizer* is illustrative. The generic drug company, Teva, filed an ANDA with respect to Pfizer's blockbuster anti-depressant, Zoloft®, in 2002. Pfizer listed two patents for Zoloft® in the Orange Book. One expired in 2006 and the other in 2010. Teva challenged only the second. That constituted an act of infringing the second patent sufficient to support an immediate infringement action by Pfizer against Teva under 35 U.S.C. § 271(e).

But Pfizer had no incentive to sue. Although Pfizer would likely do whatever it could to maintain its multi-billion dollar Zoloft® monopoly as long as possible, the 30-month stay of FDA approval was itself worth nothing to Pfizer because Teva had not challenged the patent that would expire four years later in 2006 and the FDA would not approve Teva's ANDA before that expiration, more than 30 months after Teva filed its ANDA. Moreover, by suing Teva, Pfizer

would create a risk that Teva would prevail and thereby eliminate any risk created by the patent for other generic companies. *See Teva v. Pfizer*, 395 F.3d at 1330.

When Pfizer failed to sue within 45 days of its ANDA, Teva brought an action for a declaration of invalidity and/or non-infringement of the later expiring patent. The case was justiciable under this Court's Article III jurisprudence.

Initially, if Pfizer had sued Teva under 35 U.S.C. § 271(e), the case plainly would have been a justiciable patent infringement action. Yet as this Court has ruled, "[i]t is immaterial that frequently, in the declaratory judgment suit, the positions of the parties in the conventional suit are reversed; *the inquiry is the same in either case.*" *Maryland Cas. Co. v. Pacific Coal & Oil Co.*, 312 U.S. 270, 273 (1941) (emphasis added). *See also Aetna*, 300 U.S. at 244 ("[T]he character of the controversy . . . is essentially the same whether it is presented by the insured or by the insurer. . . . It is the nature of the controversy, not . . . the particular party who presents it, that is determinative."). *See* 10B Charles A. Wright *et al.*, FEDERAL PRACTICE AND PROCEDURE § 2757, at 475 (1998) ("There is little difficulty in finding an actual controversy if all of the acts that are alleged to create liability already have occurred.").

Moreover, application of the principles set forth in *Aetna* confirmed that the controversy raised by Teva was justiciable. Teva had filed its ANDA announcing its intent to launch on the expiration of Pfizer's first Zoloft® patent. Teva's certification had statutorily infringed Pfizer's second Zoloft® patent. Its suit presented a "case admitting of an immediate and definitive determination of the legal rights of the parties." *Aetna*, 300 U.S. at 241. The controversy was "definite and concrete, touching the legal relations of parties having adverse legal interests." *Id.* at 240-41. The district court would have faced "no difficulty . . . in passing a conclusive decree applicable to the facts found and to the obligations of the

parties corresponding to those facts." *Id.* at 243. The suit called, "not for an advisory opinion upon a hypothetical basis, but for an adjudication of present right upon established facts." *Id.* at 242.

Despite the ready fit of Teva's suit under this Court's articulated criteria for Article III justiciability, and notwithstanding that this Court has "emphasized the importance to the public at large of resolving questions of patent validity,"[8] the Federal Circuit applied its "reasonable apprehension" requirement and threw out Teva's suit.

As a result of this ruling, complaints seeking to assert the "civil action to obtain patent certainty" that Congress created in 2003 are now routinely dismissed for want of subject matter jurisdiction.[9]

The Federal Circuit's decisions do not ground the "reasonable apprehension" requirement in the Article III jurisprudence of this Court. The stated rationale for the "reasonable apprehension" requirement turns, at least in substantial part, on the Federal Circuit's concern for protecting "quiescent" patentees.[10] In *Hunter Douglas, Inc. v. Harmonic*

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[8] *Cardinal Chem.*, 508 U.S. at 100.

[9] *E.g.*, *Apotex, Inc. v. Pfizer, Inc.*, 385 F. Supp. 2d 187 (S.D.N.Y.), *aff'd*, 159 Fed. Appx. 1013 (Fed. Cir. 2005), *petition for cert. filed*, 74 U.S.L.W. 3476 (U.S. Feb. 6, 2006) (No. 05-1006); *Mylan Pharm. Inc. v. Merck & Co.*, No. 05-1416, 2005 WL 2850137 (M.D. Pa. Oct. 28, 2005); *Teva Pharm. USA, Inc. v. Novartis Pharm. Corp.*, No. 05-2881, 2005 WL 3619389 (D.N.J. Dec. 12, 2005), *appeal docketed*, No. 06-1181 (Fed. Cir. Jan. 18, 2006); *Eon Labs, Inc. v. Pfizer, Inc.*, No. 05-0002, 2005 WL 1705295 (S.D.N.Y. July 19, 2005). A petition seeking review of a Federal Circuit decision affirming such a dismissal is presently pending before this Court. *Apotex, Inc. v. Pfizer, Inc.*, No. 05-1006. *Amicus* GPhA has filed in support of grant of the petition in that case.

[10] Another "part" is the Federal Circuit's asserted preference for not permitting declaratory judgments to be brought where the declaratory

*Design, Inc.*, 153 F.3d 1318, 1326 (Fed. Cir. 1998), *overruled on other grounds by Midwest Indus. v. Karavan Trailers, Inc.*, 175 F.3d 1356, 1359 (Fed. Cir. 1999), the Federal Circuit noted that it applied the reasonable apprehension requirement *because* that rule "protects quiescent patent owners against unwarranted litigation" under the patent laws. *Id.* (quoting *Arrowhead*, 846 F.2d at 736).

The desire to spare "quiescent" patentees the bother of defending declaratory judgment actions brought by parties who have made a substantial investment in potentially infringing technology may or may not be well-founded as a matter of policy,[11] but it has nothing to do with the justiciability of the controversy itself. Justiciability is a function of the underlying legal claim, regardless of which party initiates its judicial resolution. The justiciability of a claim is unaffected by the claimant's enthusiasm for asserting it, especially where the claimant insists on reserving its rights and leaving the other side up in the air.

Indeed, where the patentee has concluded that the costs of *prosecuting* patent litigation exceed the benefits of litigation, but the benefits of leaving competitors and customers uncertain as to their rights are nonetheless worth retaining, the patent has become a "scarecrow." As noted above, this Court has pointed to the "scarecrow" patent situation as a

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judgment defendant is not equally able to initiate a suit to resolve the dispute with the plaintiff. *See infra* pp. 18-20.

[11] These burdens are modest. A patentee who concludes that the declaratory judgment plaintiff's product does not infringe can easily avoid the litigation by the expedient of formally acknowledging that conclusion. Such an acknowledgment or a formal covenant not to sue the declaratory judgment plaintiff for infringement will estop the patentee from ever bringing an infringement action against the plaintiff with respect to that product and will result in the divestiture of subject matter jurisdiction. *Super Sack Mfg. Corp. v. Chase Packaging Corp.*, 57 F.3d 1054, 1059 (Fed. Cir. 1995).

paradigmatic occasion for applying the Declaratory Judgment Act. *Cardinal Chem.*, 508 U.S. at 96. Accordingly, the Federal Circuit's "reasonable apprehension of imminent suit" requirement arises out of a policy at odds with the fundamental principles of Article III as well as the legislative policy of the Declaratory Judgment Act itself.

### D. The Inability Of Genentech To Bring An Infringement Action Is No Reason To Deny MedImmune The Right To Bring A Declaratory Judgment Action.

The court of appeals declined to follow the principles of *Cardinal Chemical* in this case because Genentech, unlike the owner of a "scarecrow" patent, could not bring an infringement action because of its license to MedImmune. The court adverted to "the equalizing principles that underlie the Declaratory Judgment Act," *MedImmune*, 427 F.3d at 964, principles that the court had earlier elaborated in *Gen-Probe Inc. v. Vysis, Inc.*, 359 F.3d 1376, 1382 (Fed. Cir. 2004). In *Gen-Probe*, the Federal Circuit found it "undesirable" to permit a licensee in good standing to bring a declaratory judgment action because it would shift "all the risk" to the patentee/licensor "while the licensee would benefit from the license's effective cap on damages or royalties in the event its challenge to the patent's scope of validity fails." *Id.*

The Federal Circuit's insistence that a declaratory judgment action will lie only when the underlying infringement claim has accrued is not grounded in the Article III jurisprudence of this Court, and the Federal Circuit made no pretense to the contrary. This Court has not applied these "equalizing principles." For example, in *Maryland Casualty*, this Court permitted a liability insurance company to bring a declaratory judgment action against the plaintiff in a tort suit against the company's insured before there had been a resolution of the tort suit. The Court noted that the tort plaintiff did not have a direct action against the insurer

because the underlying tort suit had not been resolved. *Maryland Casualty*, 312 U.S. at 273. Nevertheless, despite the asymmetry of allowing the insurer to sue the tort plaintiff for a declaratory judgment when the tort plaintiff could not sue the insurer and might never be able to sue the insurer, this Court permitted the declaratory judgment action to proceed.

Moreover, this Court has frequently allowed plaintiffs to challenge the constitutionality of statutes as an alternative to violating them and raising their invalidity as a defense to an enforcement action. *Babbitt v. United Farm Workers Nat'l Union*, 442 U.S. 289, 298 (1979); *Times Film Corp. v. Chicago*, 365 U.S. 43, 45-46 (1961). Here, too, there is no application (or even consideration) of the Federal Circuit's "equalizing principles." On the contrary, the Court has recognized the advantage of applying the Declaratory Judgment Act precisely to spare plaintiffs the need to expose themselves to an enforcement action. *See Steffel v. Thompson*, 415 U.S. 452, 459 (1974). Application of the Federal Circuit's "equalizing principles" would require the dismissal of these declaratory judgment actions because the government had no corresponding ability to enforce its laws before the declaratory judgment plaintiff violated them.

The Federal Circuit itself applies these "equalizing principles" in a highly selective manner, as its treatment of declaratory judgment actions in the ANDA setting demonstrates. Congress created the "civil action to obtain patent certainty" specifically to equalize the opportunity of innovator and generic drug companies to obtain "patent certainty" before patent expiration and generic launch. District courts have routinely entertained, and the Federal Circuit has routinely reviewed, cases brought by patentees predicated upon the "technical act of infringement" of submitting an ANDA that challenges the innovator's patent. Yet the Federal Circuit ruled in *Teva v. Pfizer* that Article III precludes

the resolution of the identical controversies at the behest of generic drug companies if the patentee has not overtly threatened an infringement action.

The Federal Circuit's reliance on "equalizing principles," like its insistence on proof of a "reasonable apprehension of imminent suit," is nothing more than an attempt to engraft policy limitations, alien to this Court's jurisdiction cases, onto Article III. The Federal Circuit is wrong as a matter of constitutional law.

## CONCLUSION

The Federal Circuit's decisions in this case and other declaratory judgment actions are inconsistent with the Article III decisions of this Court, the purposes of the Declaratory Judgment Act, and the 2003 amendments to the Hatch-Waxman Act. The "reasonable apprehension" rule prevents the resolution of justiciable controversies not only in cases involving licensees but in many other patent disputes, including cases seeking to accelerate the launch of generic drugs. This Court should reverse the decision of the Federal Circuit in this case and make it clear that the "reasonable apprehension" test is not constitutionally required and may not be applied to prevent the resolution of declaratory judgment actions seeking declarations of patent invalidity or non-infringement.

Respectfully submitted,

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**Nos. 05-608**

# *In the Supreme Court of the United States*

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MEDIMMUNE, INC.,

*Petitioner,*

v.

*GENENTECH, INC. ET AL.,*

*Respondents.*

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**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

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## BRIEF OF *AMICUS CURIAE* GROUP OF LAW PROFESSORS IN SUPPORT OF AFFIRMANCE

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## BRIEF *AMICUS CURIAE* OF THE GROUP OF LAW PROFESSORS IN SUPPORT OF AFFIRMANCE

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## INTEREST OF *AMICUS CURIAE*[1]

*Amici* are scholars at American law and business schools who teach, write about, or have an interest in patent law. *Amici* have no stake in the outcome of this case, but are interested in ensuring that the law develops in a way that best promotes innovation. A full list of *amici* is appended to the signature page. Both Petitioner and Respondents have consented to the filing of this brief.

## SUMMARY OF ARGUMENT

Congress has carefully balanced the need for challenging the validity of patents with the social costs that such challenges entail. Its judgment governs this case. While statutes provide various means to challenge the validity of a patent, no statute authorizes jurisdiction under the facts raised here.

Even assuming that Congress has not addressed this issue, this Court should not allow a licensee in good standing to raise an invalidity challenge in federal court, for at least

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[1] Pursuant to Rule 37.3(a), each party consented to the filing of this brief. Those permissions accompany this brief. Pursuant to Rule 37.6, Counsel of Record certifies that no party's counsel authored this brief in whole or in part. A litigation technology company in Chicago, Illinois, 24 Seven Discovere, donated its services to print and bind this brief. This brief, however, is not submitted on behalf of 24 Seven Discovere, which has not reviewed and does not endorse its content. No other person or entity other than Counsel of Record for *amici curiae* made any monetary contribution to the preparation or submission of this brief.

three reasons. First, such challenges will result in fewer applications for letters patent. Second, it will result in less licensing of those which are sought. Third, it will upset the careful balance struck by this Court in *Lear v. Adkins* and result in a system which increases litigation by reducing the incentive to license.

## ARGUMENT

### 1. Congress Has Established Narrow Specific Means to Challenge Invalidity of Issued Patents Which Petitioner Ignores

At the outset, we concede what is obvious: there is no doubt that invalid patents are socially costly and, consequently, that challenges to patent validity should be encouraged. No doubt recognizing that fact, Congress has established three specific, settled procedures to adjudicate patent validity. In creating those procedures, Congress has balanced the benefits of more and greater invalidity challenges with other competing goals.

We show in this Section that Petitioner's challenge does not fit within any of the three common, express statutory procedures to raise invalidity.[2] Whether a fourth should be permitted is a matter for Congress, not this Court, to determine.

First, Congress has created a procedure to raise invalidity that *any person* can use, and that they can use at *any time*, but the procedure can be used only in the Patent Office (not federal court), and it can be used only to raise certain bases of invalidity. Specifically, Congress has authorized "[a]ny person at any time" to seek reexamination

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[2] Certain grounds of invalidity can be raised in other less common proceedings, such as *inter partes* interference proceedings. *See generally, Rowe v. Dror*, 112 F.3d 473 (Fed. Cir. 1997).

of an issued patent, but only in the Patent Office and only where invalidity is based upon a printed patent or other publication. 35 U.S.C. §§ 301,[3] 302;[4] *see In re Leonardo*, 119 F.3d 960, 965 (Fed. Cir. 1997) (interpreting these statutes).

Reflecting a balancing of costs and benefits, Congress did not allow *all* invalidity grounds to be raised by any member of the public, even in the less expensive, more experienced forum of the Patent Office. Instead, "[t]he legislative history indicates that considerations such as cost and availability of evidence were among the criteria

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[3] Section 301 provides in full:

> Any person at any time may cite to the Office in writing prior art consisting of patents or printed publications which that person believes to have a bearing on the patentability of any claim of a particular patent. If the person explains in writing the pertinency and manner of applying such prior art to at least one claim of the patent, the citation of such prior art and the explanation thereof will become a part of the official file of the patent. At the written request of the person citing the prior art, his or her identity will be excluded from the patent file and kept confidential.

[4] Section 302 provides in full:

> Any person at any time may file a request for reexamination by the Office of any claim of a patent on the basis of any prior art cited under the provisions of section 301 of this title. The request must be in writing and must be accompanied by payment of a reexamination fee established by the Director pursuant to the provisions of section 41 of this title. The request must set forth the pertinency and manner of applying cited prior art to every claim for which reexamination is requested. Unless the requesting person is the owner of the patent, the Director promptly will send a copy of the request to the owner of record of the patent.

Congress considered in determining the scope of reexamination." *In re Leonardo*, 119 F.3d at 965.

This appeal, however, does not involve a reexamination proceeding. (Petitioner is involved in such a proceeding, but it is not the subject of this appeal.) The basis for invalidity asserted here is not one that a member of the public could raise by way of reexamination, since it does not involve a patent or printed publication. Indeed, it goes much further since the basis for invalidity does not involve a patent or printed publication *and* Petitioner further seeks a declaration that the patent is unenforceable. (Validity and enforceability are independent concepts. *See* 35 U.S.C. § 282.)

Second, Congress has allowed for every basis of invalidity to be litigated in federal court in response to a suit for infringement. Specifically, 35 U.S.C. § 282 authorizes a party sued by a patentee for infringement – and not "any person at any time" – to raise the defense of invalidity.[5] Likewise, the same statute permits a defendant sued for infringement to raise unenforceability as a defense. *Id.* Obviously, this reflects the common sense notion that a party sued for infringement should be able to raise any invalidity or

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[5] In pertinent part, Section 282 provides:

> The following shall be defenses in any action involving the validity or infringement of a patent and shall be pleaded:
>
> (1) Noninfringement, absence of liability for infringement or unenforceability,
>
> (2) Invalidity of the patent or any claim in suit on any ground specified in part II of this title as a condition for patentability,
>
> (3) Invalidity of the patent or any claim in suit for failure to comply with any requirement of sections 112 or 251 of this title,
>
> (4) Any other fact or act made a defense by this title.

unenforceability defense as a basis for avoiding liability for infringement.

Petitioner has not been sued for infringement, however. Petitioner could not be sued for infringement, since it is a licensee in good standing.

Third, by way of the Declaratory Judgments Act, accused infringers with a reasonable apprehension of being sued for infringement may file declaratory judgment actions to establish that they do not, in fact, infringe a valid patent, or that the patent that hangs over their head is unenforceable. But such declaratory judgment arise from facts with "sufficient immediacy and reality" as to constitute a justiciable "case or controversy." *Maryland Cas. Co. v. Pacific Coal & Oil. Co.*, 312 U.S.270, 273 (1941). Thus, not any member of the public may bring a declaratory judgment seeking a determination of invalidity – only those with a reasonable apprehension of being sued.

Petitioner lacks standing to bring a declaratory judgment, since it has not been threatened with suit. Indeed, Genentech seems to lack any apparent ability to sue Petitioner since Petitioner is a licensee-in-good-standing. Section 282 simply does not authorize any person to bring a claim that a patent is invalid or unenforceable.

Petitioner plainly does not have standing under existing statutes to bring the invalidity and unenforceability claims it raises in this case, either in the Patent Office or in federal court. The existing statutory approach reflects Congress's assessment of the costs and benefits of invalidity and unenforceability determinations. Those statutes limit the scope of *what* any member of the public may raise in the Patent Office, and limits *who* may raise invalidity and unenforceability in federal court.

Petitioner, nonetheless, seeks to create a fourth procedure that goes further than Congress has deemed fit.

Congress has already decided not to permit proceedings like this, not even to members of the public in the Patent Office. It is for Congress to decide whether to allow for broader reexamination proceedings, or to extend standing beyond those authorized to raise the defense under Section 282, or to raise the issues of invalidity or unenforceability when the threat of infringement is not yet concrete and real. Whether to expand the circumstances under which invalidity and unenforceability can be adjudicated turns on a policy assessment of the costs and benefits of doing so, matters that are not best suited for judicial determination.

## II. Allowing Licensees-in-Good-Standing to Challenge the Licensed Patent Without Breach Will Lead to Less Innovation

We believe that Congress has already addressed the question presented here, and the current statutes clearly reflect its assessment of whether any member of the public should be allowed to challenge patents. This Court, should, therefore, follow the system enacted by Congress.

We also believe, however, that a rule which precludes patent owners from the benefit of having a license prevent notoriously expensive infringement suits will obviously render patent rights less valuable. The reasons are clear. The amount that a licensee will pay to use an invention will, absent unusual circumstances, be below the amount that an infringer would pay in damages for infringement. *See generally Maxwell v. J. Baker, Inc.*, 86 F.3d 1098, 1110 (Fed. Cir. 1996) (noting that an infringer should be required to pay more as "reasonable royalty" damages than a willing licensee).

A rule that permits licensees to sue the patent owner without becoming liable for the higher infringement damages obviously will increase likelihood and the amount of litigation, thus decreasing the value of patents. A decrease in value of patents, in turn, will cause fewer applicants to

disclose their inventions to obtain a patent. The fact that the grant of a license will not eliminate litigation with the licensee over invalidity (unless the licensee chooses to pay the higher damages available through infringement) means either (i) the cost of the patent will exceed its value in more circumstances, and so patents will not be sought at the margins; or (ii) a party who has the option of either obtaining patent coverage – thereby disclosing the invention to society – or of maintaining its invention through trade secret protection will, at the margins at least, opt not to obtain patent protection.

Under either option, the harm to society and to the promotion of the Useful Arts is clear: where for either reason an invention is not patented, society does not obtain disclosure of how to make and use the invention because it is not subject to patent. Thus, increasing the number of invalidity suits will decrease the incentive to disclose inventions through the patent system.

Again, while we believe that the costs of that approach outweigh the ostensible benefit of allowing more invalidity suits, whether the incremental benefit of giving licensees-in-good-standing the ability to sue for invalidity outweighs those costs is not a matter for the courts to decide. Congress has already spoken.

## III. The Rule Advocated by Petitioner Will Reduce Licensing, a Socially Desirable Activity.

Related to the foregoing, even where the inventor selects patenting, and so the public benefits from disclosure of the invention, allowing licensees-in-good-standing to unilaterally challenge the licensed patent will clearly result in less, and more expensive, patent licensing. The reasons why that is a likely consequence of a rule permitting licensees-in-good-standing to sue are straightforward.

One reason to license, of course, is that it buys peace – particularly where the license is made to conclude litigation, as was the case here. At present, a license buys peace for both parties and on all fronts. Pertinent here, a patent owner who knows, with certainty, that a license will preclude a challenge to the validity of the patent unless the licensee chooses to incur liabilities for infringement, will obviously be willing to charge less for a license, since certainty has value. *See* John W. Schlicher, *A Lear v. Adkins Allegory*, 68 J. Pat. & Trademark Off. Soc'y. 427, 434-36 (1986) (explaining how increased risk of invalidity decreases the utility of licensing and increases its costs).

A rule which permits licensees to bring invalidity suits increases uncertainty to the patentee over a rule that precludes such suits. That uncertainty necessarily will result in one or both of the following: increased license fees or fewer licenses.[6] Both are obviously troublesome consequences of a standing rule. They further can cause reduction in innovation.

We believe that Congress has already balanced these competing issues by denying a right for any member of the public to assert invalidity for any reason – either in the Patent Office or in federal court – and that absent empirical evidence otherwise, its judgment is presumptively correct: the balance struck by permitting anyone to seek

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[6] A rule which permits licensees to sue for invalidity without incurring the risk and costs that otherwise entail infringement will, at minimum, cause licensees to increase license rates to cover the additional costs created by the fact that the revenue stream from the license does not preclude a validity challenge – and loss of the asset – but *does* insulate the licensee from having to pay an amount adequate to compensate for infringement, or for the attorneys' fees incurred. *See* 35 U.S.C. § 284. *See also* 35 U.S.C. § 285 (attorneys' fees may be awarded only in 'exceptional cases' in patent suits).

reexamination coupled with the right of a party with a reasonable apprehension of being sued for infringement is the correct one.

In contrast, the rule advanced by Petitioner would result in increased licensing fees, as noted above, and less licensing. Whether that rule would increase net social good by reducing licensing is a complex question that Congress could certainly choose to address, but it plainly does not lend itself to judicial investigation. *See* Roger D. Blair & Thomas F. Cotter, *The Elusive Logic of Standing Doctrine in Intellectual Property Law*, 74 Tul. L. Rev. 1323, 1336 (2000) (explaining that "whether the innovation-enhancing effect [of licensing] outweighs the innovation-deterring effect depends on factors that may be difficult to measure and that may fluctuate from one industry to another (and from one time period to another.").

## IV. The Rule Proposed by Petitioner Upsets the Balance of *Lear*

Finally, the approach advocated by Petitioner would upset the careful balance of *Lear v. Adkins*, 395 U.S. 653 (1969), which recognized that a licensee who is sued for breaching a license agreement should be permitted to challenge the validity of the licensed patent. *Lear* recognized the inequity of permitting a patentee to claim damages for failing to pay a license without permitting the licensee to deny the validity of the claim. It allows the licensee who is attacked for breaching the license – and who, thus, as an infringer is subject to higher infringement damages and is authorized by 35 U.S.C. § 282 to raise invalidity and unenforceability as defenses – to attack back.

The clearly appropriate balance struck by *Lear* would be upset by Petitioner here. Specifically, it would allow a licensee to use a license both as a shield and sword – insulating the licensee from infringement while permitting it to attack for invalidity – and would completely unarm the

licensor, who could do nothing in response to the suit for invalidity.

Apart from its obvious inequities, this would likely reduce the amount of licensing, since it reduces the advantages that accrue to the licensee, or it would result in increased license fees to account for the fact that the patent owner is not achieving peace. Whether the decrease in licensing nets a social benefit is a question this Court should let Congress determine, but it should not adopt a rule that clearly will result in decreased licensing without a sound jurisdictional, statutory, or precedential basis to do so.

## CONCLUSION

We believe this Court should affirm the decision of the Court of Appeals of the Federal Circuit dismissing the complaint for lack of a justiciable case.

Respectfully submitted,

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In The
# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

v.

GENENTECH, INC., *et al.*,

*Respondents.*

**On Writ Of Certiorari To The United States Court Of Appeals For The Federal Circuit**

## BRIEF OF *AMICUS CURIAE* LICENSING EXECUTIVES SOCIETY (U.S.A. & CANADA), INC. IN SUPPORT OF NEITHER PARTY

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## STATEMENT OF INTEREST[1]

The Licensing Executives Society (U.S.A. & Canada), Inc. ("LES") is a non-profit professional society comprised of over 6,000 members engaged in the transfer, use, development, manufacture and marketing of intellectual property. LES's members include a wide range of professionals, including business executives, lawyers, licensing consultants, engineers, academicians, scientists and government officials, all of whom are engaged in the licensing of intellectual property. Members are employed by many large corporations, professional firms and universities. LES's purposes include: encouraging high standards and ethics among persons engaged in domestic and international licensing and transfers of technology and intellectual property rights; and assisting its members in improving their skills and techniques in those fields. With this broad-based constituency, LES is directly interested in the impact this Court's decision will have on the licensing of intellectual property, and patents in particular.

LES has received the consent of the parties in this case to file this brief.

## SUMMARY OF ARGUMENT

While this case directly concerns whether a patent licensee must materially breach a license agreement in order to bring a declaratory judgment action for invalidity

[1] Counsel for a party did not author this brief in whole or in part. No person or entity, other than the *Amicus Curiae*, its members, or its counsel made a monetary contribution to the preparation and submission of this brief.

of the licensed patent, it also highlights the uncertainty as to the vitality of the doctrine of *Lear v. Adkins*, 359 U.S. 653 (1969). This Court, in *Lear*, held that licensees could not be precluded from challenging the validity of a licensed patent under the doctrine of licensee estoppel. The progeny of *Lear*, however, have left licensees and licensors uncertain as to its effect.

Licensees and licensors now often do not know prior to entering into a license agreement whether, when, or how licensees will be permitted to challenge patent validity. Similarly, licensees and licensors often do not know to what extent licensors can prevent, hinder, or ameliorate the impact of such validity challenges. As with any contract, in order to ensure that each party to a license agreement receives its bargained for benefits, the parties should understand from the outset their full rights and liabilities under the license agreement. Without knowing what right a licensee has to challenge the validity of the licensed patent or what right a licensor has to prevent such a challenge or to terminate the agreement in the face of such a challenge, licensees and licensors cannot be certain as to the full scope of the bargained for exchange. Thus, both patent licensees and licensors have an interest in knowing with certainty the consequences of entering into a license agreement. The Court is now in a position to resolve uncertainty in this area by issuing a ruling that clarifies and explains the continuing validity and scope of the *Lear* doctrine. LES urges the Court to provide such clarity.

## ARGUMENT

### I. IN *LEAR V. ADKINS*, THIS COURT REJECTED THE DOCTRINE OF "LICENSEE ESTOPPEL"

The issue presented in this case is whether a licensee in good standing may bring a declaratory judgment action for patent invalidity. At its core, this issue has its roots in the doctrine of licensee estoppel, a doctrine that has existed in the United States since at least the middle of the nineteenth century. *See Lear*, 395 U.S. at 662. The concept of estopping a licensee from challenging patent validity is based on the principle of contract law that a purchaser may not "repudiate his promises simply because he later becomes dissatisfied with the bargain he has made." *Id.* at 668. In several cases in the early twentieth century, this Court upheld the application of licensee estoppel. *See U.S. v. Harvey Steel Co.*, 196 U.S. 310, 317 (1905); *Automatic Radio Mfg Co. v. Hazeltine Research, Inc.*, 339 U.S. 827, 836 (1950).

In 1969, however, this Court rejected the doctrine of licensee estoppel as conflicting with the "important public interest in permitting full and free competition in the use of ideas which are in reality a part of the public domain." *Lear*, 395 U.S. at 670-71. This Court further held that licensees are the only parties with sufficient economic incentive to challenge the validity of a patent, and therefore, if "muzzled," the public would be forced to pay for technology that should rightly be free for all to use. *Id.*

This Court also addressed whether a licensee could be required to pay royalties while it challenged the validity of a patent. *Id.* at 673. The Court found it "inconsistent with the aims of federal patent policy" to require a licensee to pay royalties during such a challenge. *Id.* In particular,

the Court expressed concern that such a requirement would deter licensees from bringing validity challenges. *Id.*

Commentators' responses to *Lear* were mixed. *See, e.g,* Rochelle C. Dreyfus, *Dethroning Lear: Licensee Estoppel and the Incentive to Innovate*, 72 Va. L. Rev. 677, 686-87 (1986) (discussing mixed response to *Lear*). Although the decision provided some certainty regarding the consequences of entering into a license agreement, it was unclear how broadly the decision would be applied.

For example, it was unclear whether *Lear* applied to all patent license agreements or only to non-exclusive license agreements such as those at issue in *Lear*. Further, because the estoppel negated in *Lear* was implied and not express in the contract, it was unclear whether a party could explicitly contract away its right to challenge patent validity. Moreover, if that estoppel did preclude an express contractual restriction, could a licensor provide a clause allowing for termination in the event of a validity challenge? Finally, while this Court held that a licensee could not be required to pay royalties during a validity challenge, it did not address whether a licensee could continue to pay royalties and still challenge the validity of the licensed patent.

## II. SINCE THE *LEAR* DECISION, THE COURTS OF APPEALS HAVE PROVIDED UNCERTAIN GUIDANCE TO CONTRACTING PARTIES

Following this Court's decision in *Lear*, the various courts of appeals attempted to resolve the various issues discussed above. While many of these issues were resolved without controversy, others remain uncertain to this day.

### A. The Courts of Appeals Have Provided Uncertain Guidance as to the Types of Agreements to Which *Lear* Applies.

Understanding the breadth of *Lear* is important for both licensees and licensors. Contracting parties need to know with certainty whether or not a promise not to challenge the validity of a patent in an agreement will be enforceable in advance of entering into an agreement. The enforceability of such a clause can be a significant form of consideration for a licensor and can greatly impact the negotiation of an agreement as a whole. Similarly, even if a licensee does not expressly promise not to challenge validity, it would benefit both licensees and licensors to know at the time they enter into an agreement when and how that licensee could challenge the validity of the licensed patent. Each party to the agreement would likely value the agreement differently if it knew that a licensee could challenge validity at any time or if it knew the licensee could not challenge validity and maintain the license.

For certain types of agreements, courts have applied *Lear* consistently. For example, *Lear* itself involved a non-exclusive license agreement, so licensees under such agreements have generally been able to rely on the protection provided by *Lear*. The courts of appeals have also held that *Lear* applies not only to non-exclusive license agreements, but also to exclusive license agreements. *See, e.g., Beckman Instruments, Inc. v. Technical Dev. Corp.*, 433 F.2d 55, 58 (7th Cir. 1970).

For other types of agreements, the guidance provided by the courts of appeals has been less clear. One such agreement is a consent judgment. Following *Lear*, several circuit courts of appeals held that the *res judicata* effect of

a consent judgment outweighed the policy concerns expressed by this Court in *Lear*, and therefore, enforced consent judgments precluding a licensee from challenging patent validity. *See, e.g., Interdynamics, Inc. v. Firma Wolf*, 653 F.2d 93, 97-98 (3rd Cir. 1981); *Schlegal Mfg. Co. v. USM Corp.*, 525 F.2d 775, 779-81 (6th Cir. 1975). The Seventh Circuit, however, found such a holding to be inconsistent with *Lear* and held that a "licensee, is not estopped from challenging the validity of the patent, even though a prior consent decree incorporated an understanding not to challenge the validity of the patent." *Kraly v. Nat'l Distillers and Chem. Corp.*, 502 F.2d 1366, 1369 (7th. Cir. 1974).

In 1982, the Court of Appeals for the Federal Circuit was formed and given exclusive jurisdiction over claims arising under the patent laws. Therefore, for the past 20 years, most, if not all, appeals addressing the issues raised in *Lear* have passed through the Federal Circuit. The Federal Circuit has consistently held that a consent judgment can act as a bar to future validity challenges. *See, e.g., Diversy Lever, Inc. v. Ecolab, Inc.*, 191 F.3d 1350, 1352 (Fed. Cir. 1999); *Foster v. Halco Mfg., Inc.*, 947 F.2d 469, 476-77 (Fed. Cir. 1991). While the Federal Circuit's consistency has removed some of the uncertainty regarding consent judgments, some uncertainty remains given the suggestion by the Seventh Circuit that the policy underlying those decisions conflicts with *Lear*.

Since the *Lear* decision, it has also not always been clear to what extent *Lear* applies to settlement agreements. When applying *Lear*, the Ninth Circuit has stated that making a distinction between a settlement agreement and a license agreement is "unworkable," because "it would be . . . easy to couch licensing arrangements in the

form of settlement agreements." *Massillon-Cleveland-Akron Sign Co. v. Golden State Adver. Co.*, 444 F.2d 425, 427 (9th Cir. 1971). The Ninth Circuit, therefore, held that *Lear* applied to a "settlement agreement" entered into before a litigation had been filed. *Id.* When addressing settlement agreements, the Federal Circuit has drawn a distinction between agreements entered into before litigation and those entered into after litigation, holding that a licensee can be estopped from challenging patent validity in an agreement settling actual litigation. *See, e.g., Flex-Foot, Inc. v. CRP, Inc.*, 238 F.3d 1362, 1369-70 (Fed. Cir. 2001). In so holding, the Federal Circuit found that the policy of encouraging settlement of litigation outweighs the public policy concerns expressed by this Court in *Lear*. The Federal Circuit has not clarified, however, whether the mere filing of a litigation prior to settlement is sufficient to take a settlement agreement outside of *Lear* or whether the contracting parties need to have more fully litigated the case for the policy favoring settlement of litigation to outweigh the public interest in having the validity of patents tested.

The need for further clarification on the extent to which the policies favoring settlement outweigh those expressed in *Lear* is illustrated by a recent case from the District Court for the Eastern District of Michigan. In *Warrior Lacrosse, Inc. v. Brine, Inc.*, No. 04-71649, 2006 WL 763190 (E.D. Mich. March 8, 2006), a licensee was estopped from challenging the validity of a patent licensed in a settlement agreement despite the fact that the settlement occurred in the very early stages of the litigation. 2006 WL 763190, at *25.

In *Warrior Lacrosse*, a licensee sought to challenge the validity of a patent licensed in connection with a litigation

settled in the early stages of the case. 2006 WL 763190, *23-27. The special master in *Warrior* held that the Federal Circuit's decision in *Flex-Foot*, 238 F.3d 1362, required that a licensee who waives the right to challenge the validity of a patent in an agreement settling litigation be estopped in any future action from challenging the validity of the licensed patent. 2006 WL 763190, at *24-25. The *Warrior* licensee argued that *Flex-Foot* was distinguishable because, in that case, the settlement had been entered into after extensive discovery and summary judgment briefing, while the litigation at issue in *Warrior* concluded in its early stages with little discovery and no summary judgment proceedings. *Id.* at *25. The special master concluded that the Federal Circuit placed no requirement on when in litigation the settlement must occur. *Id.* at *26. Moreover, the special master viewed the aims of judicial economy as better served by early settlement. *Id.* As a result, the special master found the licensee estopped from challenging validity. *Id.*

In *Warrior*, the special master interpreted the Federal Circuit's holding in *Flex-Foot* to mean that any settlement of litigation can result in licensee estoppel. *Id.* at *25. Under this interpretation, a license agreement reached after several years of negotiation could not be used to estop a licensee from challenging patent validity, while a "settlement agreement" reached after only a few weeks of litigation could. As a result of such a ruling, litigation can be used as a tactic to circumvent this court's holding in *Lear*. On the other hand, the filing of a suit is a known and identifiable event that can provide a bright line regarding the application of *Lear* to settlement agreements.

### B. The Courts of Appeals Have Not Provided Guidance as to the Enforceability of Clauses Providing Only Impediments, but not Absolute Bars, to Validity Challenges.

The agreement at issue in *Lear* did not have a clause expressly precluding validity challenges. Subsequent to *Lear*, however, the courts of appeals have consistently held that a clause in a license agreement expressly prohibiting a licensee from challenging patent validity is unenforceable. *See, e.g.*, *Massillon*, 444 F.2d at 427. While it is clear that, if *Lear* applies to an agreement, a licensor cannot contractually prohibit a licensee from challenging patent validity, it is unclear to what extent, if any, a licensor can provide an impediment to such a challenge. This is important to both licensees and licensors, as the ability to hinder or impede, if not bar, a validity challenge could substantially affect the negotiation of a license agreement.

For example, none of the courts of appeals have directly addressed whether a clause in a license agreement providing for termination in the event of a challenge to patent validity would be enforceable.[2] While such a clause may be viewed as a barrier to a licensee's validity challenge, it would at the same time provide some protection

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[2] In *Bayer AG v. Housey Pharms., Inc.*, 228 F. Supp.2d 467 (D. Del. 2002), the U.S. District Court for the District of Delaware was faced with a clause in a license agreement permitting termination if the licensee challenged the validity of the licensed patent and which also included a provision requiring the licensee to pay royalties during a validity challenge. *Id.* at 474. The court found the portion of the agreement requiring the payment of royalties during a challenge to validity to be unenforceable under *Lear*, but was silent as to the enforceability of the remainder of the clause. *Id.* This aspect of the decision was not appealed.

to the licensor where the licensee expressly contracts away the right to challenge validity while maintaining the license. Moreover, such a clause does not prevent a licensee from bringing a validity challenge, but only requires a licensee to choose between maintaining its license or bringing a validity challenge. Similarly, no courts have yet addressed whether a licensor could charge a higher royalty rate should a licensee bring a validity challenge. Again, such a clause might act as an impediment to a validity challenge, but would not act as an absolute bar. Both licensees and licensors have an interest in understanding the extent to which such provisions can be enforced under *Lear*.

### C. The Courts of Appeals Have Not Provided Clear Guidance as to When a Licensee may Invoke *Lear* to Bring Suit to Challenge Validity.

The Federal Circuit and other courts of appeals have taken differing approaches to the issue at the heart of the present case – whether a licensee in good standing has standing to bring a declaratory judgment action for invalidity. Prior to the formation of the Federal Circuit, the courts of appeals were generally split on whether a license agreement must be terminated in order for a licensee to bring a declaratory judgment action. *Compare Thiokol Chem. Corp. v. Burlington Indus., Inc.*, 448 F.2d 1328, 1330-31 (3rd Cir. 1971) (holding that while a license agreement is in place no threat of infringement exists) *with Warner-Jenkinson Co. v. Allied Chem. Corp.*, 567 F.2d 184, 187-88 (2nd Cir. 1977) (finding a case or controversy even though licensee had not ceased paying royalties under the license agreement).

The Federal Circuit has never held that a licensee in good standing may, in all cases, challenge the validity of a licensed patent. However, the Federal Circuit has indicated that licensees should not be discouraged from challenging the validity of a licensed patent by being put at risk for infringement. *C.R. Bard, Inc. v. Schwartz*, 716 F.2d 874, 880 (Fed. Cir. 1983). In that vein, the Federal Circuit rejected any bright line rule requiring termination of a license agreement in order to challenge validity, stating:

> We reject the blanket approach of *Thiokol* that there can never be an apprehension of a federal infringement suit and thus no controversy when a license is still in effect. To always require the termination of a license agreement as a precondition to suit would mean that a licensee must then bear the risk of liability of infringement. This would discourage licensees from contesting patent validity and would be contrary to the policies expressed in *Lear*.

*Id.* Instead, the Federal Circuit applied a "totality of the circumstances" test to determine whether an actual controversy existed. *Id.* Doing so, the Federal Circuit found an actual controversy based on the fact that the licensee had stopped paying royalties, and the agreement, therefore, could have been terminated. *Id.* at 880-81.

More than 20 years later, in *Gen-Probe v. Vysis*, 359 F.3d 1376 (Fed. Cir. 2004), the Federal Circuit suggested that licensees should not be permitted to challenge the validity of a licensed patent unless they are at risk for infringement. The Federal Circuit held in that case that a licensee could not bring a declaratory judgment action for patent invalidity without materially breaching the license

agreement. *Id.* at 1381. Noting that "the *Lear* doctrine . . . does not grant every licensee in every circumstance the right to challenge the validity of the licensed patent," the court expressed concern regarding the potential inequity of allowing a licensee to both maintain its license and simultaneously seek to invalidate the licensed patents. *Id.* at 1381-82. The Federal Circuit believed that such a result would require the licensor to "bear all the risk" and might discourage patentees from granting licenses. *Id.* at 1382. Thus, while the holding in *Gen-Probe* is not inconsistent with the holding in *C.R. Bard*, the tenor of the two cases is quite different, suggesting in one that licensees should be encouraged to challenge validity and noting in the other that licensees do not have an unfettered right to challenge validity and leaving licensees and licensors uncertain as to how and when validity may be challenged.

The *Gen-Probe* decision provides a bright-line rule that is easy to apply and follow. In this regard, the licensing community benefits from increased certainty. At the same time, however, *Gen-Probe* seems to be at odds with some of the policy concerns expressed by this Court in *Lear*. Specifically, while this Court in *Lear* was concerned with "unmuzzling" licensees, the *Gen-Probe* rule may have the effect of discouraging licensees from bringing validity challenges as the Federal Circuit itself suggests in *C.R. Bard*. The Second Circuit expressed similar concern in *Warner-Jenkinson*, stating:

> A licensee who wishes to continue using the patented element cannot withhold royalty payments without laying himself open to large potential liability for infringement and an injunction against all future use of the patented substance. If forced to make the hard choice, many licensees

> will choose the less perilous course, and the patents under which they are licensed will remain uncontested. *Lear* established that removing restraints on commerce caused by improperly-held patents should be considered more important than enforcing promised between contracting parties. Thus, the seeming inequity of allowing a licensee to keep his license while he attacks the validity of the licensor's patent is outweighed by the public interest in placing no impediment in the way of those in the best position to contest the validity of the underlying patent.

*Id.* at 187-88.

In addition, this issue has been made less clear by the fact that the courts of appeals, including the Federal Circuit, have rendered many decisions that expressly or impliedly permitted licensees to continue to pay royalties during a validity challenge, when the issue of declaratory judgment jurisdiction was not raised.

For example, some courts have held that *Lear* entitles a licensee to make payments to the licensor during a challenge to validity, and then recoup those royalties if successful. *See Warner-Jenkinson*, 567 F.2d at 188. Other courts have permitted the licensee to make payments into an escrow account pending the outcome of a validity challenge. *See Atlas Chem. Indus., Inc. v. Moraine Prods.*, 509 F.2d 1, 7 (6th Cir. 1977). The Federal Circuit, on the other hand, has said that a court cannot enjoin a licensor from terminating a license agreement where the licensee is paying royalties into escrow and not to the licensor. *See Cordis Corp. v. Medtronic, Inc.*, 780 F.2d 991, 995 (Fed. Cir. 1985). In *Cordis*, however, the Federal Circuit cited with approval the portions of *Warner-Jenkinson* indicating

that a licensee could pay royalties to the licensor during a validity challenge. *Id.*

More recently, however, the Federal Circuit held that a licensee cannot pay royalties at all during a validity challenge. *See Studingesellschaft Kohle, M.B.H. v. Shell Oil Co.*, 112 F.3d 1561, 1568 (Fed. Cir. 1997). In *Kohle*, the Federal Circuit held that a licensee is liable for royalties due under a license agreement until (1) it actually ceases the payment of royalties and (2) provides notice that the reason for ceasing payment is a claim of patent invalidity. *Studingesellschaft Kohle, M.B.H. v. Shell Oil Co.*, 112 F.3d 1561, 1568 (Fed. Cir. 1997). Therefore, a licensee may be liable for royalties due even under an invalid patent until it actually takes these two steps. *Id.*

As a consequence of the apparent tension created by *Gen-Probe* and the unclear law on the payment of royalties during validity challenges, the law in the area of patent licensing is less certain. Both patent licensees and licensors now have less certainty as to when a licensor will be able to challenge validity, what must be done to challenge validity, and whether a licensee can pay royalties during a challenge to validity and maintain the license.

One recent district court decision demonstrates this uncertainty. In *Advanced Card Techs. LLC v. Versatile Card Tech., Inc.*, 410 F.Supp.2d 158, (S.D.N.Y. 2006), a licensee was estopped from challenging patent validity in a suit to collect royalties even though the claims of the patents at issue had been cancelled by the U.S. Patent & Trademark Office during reexamination of the patents and even though the licensor had admitted that those claims were invalid. 410 F. Supp.2d at 160-61.

The licensee in *Advanced Card* disputed that certain of its products were covered by the licensed patents and thus refused to pay royalties on those products. 410 F. Supp.2d at 160-61. The licensee did not contend at that time that the patents were invalid and therefore continued to pay royalties on the products it acknowledged were covered by the licensed patents. *Id.* at 160. When the licensor sued to collect the royalties due, the licensee counterclaimed for invalidity, asserting that the patents were invalid because the claims in those patents had been cancelled during reexamination proceedings. *Id.* The district court relied on the Federal Circuit's decision in *Studingesellschaft Kohl*, 112 F.3d 1561, where the court held that a licensee was liable for royalties due under an invalid patent until it stopped royalties and notified the licensor that the royalties were not being paid based on a claim of invalidity. *Id.* at 161. Because the licensee in *Advanced Card* only refused to pay royalties on some products and then only based that refusal on a claim of non-infringement, the district court held that licensee estoppel would apply and the licensee could not challenge the validity of the licensed patents. *Id.* at 161.

Thus, in *Advanced Card*, the licensee was estopped from challenging validity even though it had stopped paying royalties and even though the claims were admittedly invalid. *Id.* While the facts of *Advanced Card* are certainly distinguishable from *Lear*, at its core, the result of that case was that a licensee under a nonexclusive license agreement was estopped from challenging patent validity in a suit seeking to collect royalties. The district court expressed surprise at the licensee's unwillingness to cease payment for all products, 112 F.3d at 162, perhaps not recognizing that the licensee did not wish to have the

license terminated for those products that it conceded were covered by the patent or might be covered by new claims that were to issue.

## III. GUIDANCE IS NEEDED FROM THIS COURT TO PROVIDE CERTAINTY REGARDING THE APPLICATION OF LICENSEE ESTOPPEL IN PATENT LICENSE AGREEMENTS

The decisions discussed above demonstrate the need for this Court to provide guidance in the area of licensee estoppel. In the present case, this Court has the opportunity to clarify the continuing scope and effect, if any, of the *Lear* doctrine. First, the Court can either reaffirm the continuing validity of the *Lear* doctrine or overrule that doctrine once and for all. Second, the Court can provide certainty with respect to the reach of *Lear* and the requirements for a licensee's challenge to patent validity. LES does not urge a particular ruling from this Court on these issues. LES only asks that the Court provide licensees and licensors the ability to readily determine when licensee estoppel will apply and when a licensee can bring an action to challenge patent validity.

In addition, if the Court overturns the Federal Circuit's requirement that a licensee materially breach a license agreement in order to challenge patent validity, LES requests that the Court provide further guidance on exactly what is required to bring a challenge to validity. In other words, can any licensee challenge validity or must it first demonstrate some actual dispute?

As noted above, there are also several issues that could remain unsettled if this Court finds that *Lear* permits a licensee in good standing to challenge validity.

For instance, does *Lear* prohibit any impediment to challenging the validity of a licensed patent? For example, can a licensor include a clause in an agreement permitting termination in the event of a challenge to patent validity? While such a clause may be viewed as potentially discouraging licensees from challenging validity, it would at the same time provide some protection to the licensor where the licensee expressly contracts away the right to challenge validity while maintaining the license. Alternatively, can a licensor establish different royalties based on whether the licensee challenges validity? While a higher royalty rate following a validity challenge could also be viewed as a disincentive to the licensee, the licensee would not be barred from challenging validity and the licensee could keep the license. At the same time, the higher royalty rate could take some of the risk off of the licensor and could be an acknowledgement of at least some of the costs associated with defending the validity of the licensed patent.

In addition, if a licensee can continue to pay royalties during a validity challenge, another issue that remains is whether a licensee can seek a refund of the royalties paid after a challenge to validity. In that situation, there would be less incentive for the licensee to challenge validity early since it could simply wait and attempt to recoup the royalties paid many years later, thus frustrating the policy underlying *Lear*. Alternatively, can a licensee pay royalties into an escrow account during a validity challenge?

Finally, yet another issue is whether a licensee in good standing can challenge issues other than the validity of a licensed patent, such as whether the licensee does not infringe that patent. This Court has stated that the public has an interest in having the validity of patents tested,

but this Court has not discussed whether any such public interest exists with respect to infringement. A licensee's interest in having infringement adjudicated would appear to be a personal one. Thus, even if this Court considers it fair to allow a licensee in good standing to challenge validity, a question remains as to whether it is fair to allow that licensee to challenge infringement. LES requests further guidance on these issues.

## CONCLUSION

For these reasons, the Licensing Executives Society (U.S.A. & Canada), Inc. requests that the Court's ruling in this case provide the certainty desired by licensees and licensors in the area of licensee estoppel.

Respectfully submitted,

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May 15, 2006

No. 05-608

# In the Supreme Court of the United States

MEDIMMUNE, INC.

*Petitioner,*

v.

GENENTECH, INC., *ET AL.*,

*Respondents*

*ON A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT*

## BRIEF OF AMICUS CURIAE MEDTRONIC, INC. IN SUPPORT OF PETITIONER

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## Interest of the *Amicus*

This brief is filed with the consent of the parties[1] on behalf of Medtronic, Inc. Medtronic is the world leader in medical technology providing lifelong solutions for people with chronic disease. It offers a variety of medical products, therapies and services that enhance or extend the lives of millions of people. Each year, patients benefit from Medtronic's technology, used to treat conditions such as diabetes, heart disease, neurological disorders, and vascular illnesses. Because the medical devices industry has a large number of patents, many of them overlapping. Medtronic is frequently a party to patent litigation.

Medtronic's interest in this case arises from one of those litigations. As the Court knows, patent litigation involves issues that are often very complicated, both from a technical and a legal perspective. Medtronic sometimes finds that the most reasonable business solution to patent litigation is to enter into a licensing agreement, despite continuing differences between the parties as to the scope or validity of the claims. Medtronic believes that the standing decisions that have recently emerged from the Court of Appeals for the Federal Circuit are inconsistent with this Court's well-established case-and-controversy principles and

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[1] The parties' letters of consent have been filed with the Clerk in compliance with Rule 37.3. This brief was not authored in whole or in part by counsel for any party. No person or entity other than the *amicus* made a monetary contribution to the preparation or submission of this brief.

will prevent parties from reaching the most efficient business solution to patent disputes.

Medtronic has an appeal pending before the Federal Circuit that touches on the Question Presented in this case.[2] Medtronic believes that the facts of that case and of a similar prior Medtronic appeal to that court serve as a useful backdrop for illustrating the legal and practical problems raised by the decision under review in this case.

## Summary of Argument

The Federal Circuit's rule of decision that precludes a patent licensee in good standing from seeking a declaratory judgment that the patent is invalid fails to follow the principles established by this Court in *Aetna Life Insurance Co. v. Haworth*, 300 U.S. 227 (1937) and *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969). The circuit's rule appears to draw a distinction between cases where disputed royalty payments are escrowed and cases where the licensee continues to pay royalties on a current basis. There is no valid reason in either situation to dismiss invalidity claims brought by licensees on the ground that there is no case or controversy within the Article III jurisdiction of the federal courts.

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[2] The pending appeal is *Medtronic v. Guidant, et al.*, CAFC No. 05-1515. The case was argued and submitted to the Federal Circuit on May 4, 2006.

## Argument

### I. Medtronic's Experience in Litigating Declaratory Judgment Actions as a Patent Licensee Before the Federal Circuit May Assist the Court To Decide this Case

The declaratory judgment issue presented in this case has arisen in two cases Medtronic has argued before the Court of Appeals for the Federal Circuit, one of which is pending there now. Those two cases present a factual variation on licensee standing that the Federal Circuit has previously found significant. In both cases a licensee in good standing did not merely dispute the scope or validity of its license, it ceased paying royalties to the licensor and instead paid them into an escrow pending final determination of a declaratory judgment action to resolve the dispute. Medtronic agrees with the Petitioner that the recent Federal Circuit decisions on this issue were wrongly decided, but believes this Court may wish to consider the significance of a contemporaneous royalty escrow when it decides this case.

The Question Presented has its roots in the Federal Circuit's decision in *Gen-Probe, Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir. 2004). The panel opinion in that case did discuss this Court's highly decisions in *Aetna* and *Lear*, although it failed to properly apply them. The *Gen-Probe* decision did not, however, discuss that court's own prior decision in *Cordis, Corp. v. Medtronic, Inc.*, 835 F.2d 859 (Fed. Cir. 1987) which found that there was a case and controversy sufficient to sustain jurisdiction to issue a declaratory judgment in a case brought by a Medtronic licensee in good standing.

*Cordis* arose from a patent license Medtronic had

granted to Cordis for pacemaker leads. Cordis was manufacturing one variety of leads under that license and was paying royalties on those leads. Cordis later developed a new lead that it claimed was not covered by the patent; Medtronic disagreed and said it would cancel the license agreement if Cordis refused to pay royalties on future sales of the new leads. Medtronic also reserved a claim to sue for past infringement from prior sales. In light of those assertions, Cordis instituted a declaratory judgment action seeking a preliminary injunction to prevent Medtronic from canceling the license and asking for a declaration that the new leads were not covered by the patent or the license agreement. Cordis also immediately "moved for an order to establish an escrow account into which the royalty payments due Medtronic on the [new] leads could be deposited during the litigation . . . ." 835 F.2d at 861. On those facts the Federal Circuit found that there was a case and controversy within the meaning of Article III. *Cordis* 835 F.2d at 863. The panel relied on prior decisions in concluding that Cordis was "under a reasonable apprehension or threat of being sued for infringement." *Id.* at 862.

*Gen-Probe* arose from a somewhat similar fact pattern, but it differed from *Cordis* in that it did not involve any escrow of disputed royalties. Gen-Probe and Vysis were adversaries in litigation involving a number of patents. During that litigation, Vysis obtained ownership of an unrelated patent which it claimed covered certain Gen-Probe products. Gen-Probe took a license under that patent, but then initiated a declaratory judgment action that the patent did not cover the products and was invalid. Throughout the pendency of that suit Gen-Probe "fulfilled its obligations [under the license] and continued paying royalties." *Gen-Probe*, 359 F.3d at 1379. In that case the Federal Circuit held that there was no case and controversy and dismissed the appeal, finding "there is not a reasonable

apprehension of suit." *Id.* at 1382.[3]

Medtronic's more recent experience before the Federal Circuit involving this issue arose in the context of a dispute over the scope and validity of certain cardiac pacemaker patents. Medtronic was a party to six separate litigations where the owner and exclusive licensee of the numerous patents contended that certain Medtronic pacemakers and defibrillators infringed several patents. In 1991, Medtronic settled those lawsuits and took a license, while specifically reserving the right to contest the application, validity and enforceability in subsequent declaratory judgment actions. When a dispute later arose over one of the licensed patents, Medtronic denied any obligation to pay royalties, in part on the basis of a claim of invalidity because claims surrendered in the prosecution of the original patent had been improperly recaptured in a reissue of that patent. Medtronic filed a complaint seeking a declaratory judgment in the United States District Court for the District of Delaware as provided for in the settlement agreement. Prior to institution of the action, the parties agreed to escrow all royalty payments the owner asserted were due by virtue of the reissue claims. That escrow continues to this day and the amount on deposit exceeds $5,000,000.

The District Court concluded that it did have jurisdiction and issued a final judgment on July 19, 2005 finding the patent valid. *Medtronic, Inc. v. Guidant Corp.*,

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[3] The Federal Circuit relied on and followed the *Gen-Probe* decision in dismissing this case and a similar one, *MedImmune v. Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005), *cert. pending* in 05-656.

378 F. Supp 2d 503 (D. Del. 2005). That case differed from *Gen-Probe* and this case because of the escrow of royalties. On appeal Medtronic contended that the case was substantially similar to its prior dispute with Cordis because of the presence of an escrow and the prior litigation between the same parties involving the same patent. The jurisdictional issue presented here was raised and discussed in Medtronic's briefs and oral argument in the Federal Circuit where the case remains under consideration by the panel as of the filing of this *amicus* brief.

## II. The Declaratory Judgment Action Is An Important Alternative that Potential Licensees Need to Avoid Excessive Infringement Litigation

Unless this Court reverses the Federal Circuit and clarifies the law to make it clear that patent licensees can bring declaratory judgments to challenge the validity of questionable patents, potential licensees will be forced to defend more patent litigations, a result that will increase docket congestion. This reality is particularly acute in the technology and medical device industries that are characterized by a multiplicity of patents.

The license agreement that is involved in the pending Medtronic/Guidant case is typical of agreements in the medical device and technology industries today. That settlement and licensing agreement licensed over 500 US patents and pending applications. In many industries, the single patent license agreement is the exception and not the rule. More often, companies cross-license dozens or hundreds of patents to a defined set of licensed products or in a licensed field of use. This is particularly true of cross-license agreements resulting from settlement of patent

litigation. If a company cannot enter into a comprehensive settlement and licensing agreement except at the cost of being unable to challenge the validity of individual questionable patents, it will face the Hobson's choice of foregoing a settlement in order to preserve challenges to some of the patents, or accept a settlement that precludes judicial determination of the validity of those patents.

Neither of those alternatives serves the public or private interests. Under the present Federal Circuit rule patents of dubious validity will remain unchallenged if the affected entity enters into a comprehensive patent licensing agreement. On the other hand, if that party declines to enter into such an agreement in order to maintain the ability to challenge those patents, it is likely to become a defendant in suits brought on other patents in the patentee's portfolio, suits that could be avoided or resolved through a comprehensive settlement. The realities of today's technology driven society present the multi-patent licensing concept as the norm in many industries. If the Federal Circuit's rule stands, parties in Medtronic's position are put at risk of losing all patents included in a license agreement to challenge a dispute over one or a few patents. As a practical matter, the licensee has no remedy whatsoever if the parties cannot enter into a comprehensive settlement while agreeing to continue resolving genuine disputes involving a small number of the patents through the courts

## III. The Precedent in the Court of Appeals for the Federal Circuit Are Inconsistent with This Court's Decisions

The recent Federal Circuit cases that have refused to find jurisdiction when a licensee in good standing contests the claim scope or validity of its license are inconsistent with

this Court's fundamental declaratory judgment decisions, as well as the policy rationale that undergirds the decision in *Lear v. Adkins, supra.*

### *A. The Federal Circuit Decisions Fail to Follow the Well-Established Principle that a Case and Controversy Sufficient to Sustain Jurisdiction Exists When the Parties to a Contract Have a Bona Fide Dispute Over its Proper Interpretation.*

The Declaratory Judgment Act was enacted in 1934 in part to facilitate parties' ability to resolve legal disputes. Prior to creation of the declaratory judgment remedy, disputes could arise where someone asserted a legal right but declined to enforce it through litigation seeking a money judgment or injunction. The declaratory judgment remedy met the need that the putative defendant in a coercive action had to resolve that legal dispute. An essential part of the federal remedy was the requirement that it can only be invoked where there is an actual case or controversy.

The lower federal courts were not uniformly receptive to the declaratory judgment procedure. One of the earliest cases involving the Act that the Court considered is one of the most pertinent for the decision in this case.

*Aetna v. Haworth* arose from a dispute between an insurance carrier and its insured over the coverage of disability benefits. The insured had ceased making payments, claiming he was totally disabled and entitled to the benefits without paying any additional premiums. The carrier disputed the validity of the disability claim. The insured never brought an action to recover the claimed benefits, so the carrier instituted an action in federal court seeking a declaratory judgment that there was no disability.

The trial court dismissed the carrier's complaint finding there was no controversy within the meaning of Article III. 200 U.S. at 236. The Circuit Court affirmed. *Id.* This Court, in a unanimous opinion authored by Chief Justice Hughes, reversed and held that there was a case and controversy that sustained federal jurisdiction and was within the scope of the then recently-enacted Federal Declaratory Judgment Act. The Court's rationale was succinct and unambiguous:

> There is here a dispute between parties who face each other in an adversary proceeding. The dispute relates to legal rights and obligations arising from the contracts of insurance. The dispute is definite and concrete, not hypothetical or abstract.

200 U.S. at 242

*Aetna* remains a cornerstone of declaratory judgment precedents. When the Federal Circuit decided *Gen-Probe* it discussed *Aetna* and distinguished it on the grounds that it was an insurance dispute and "did not involve a declaratory judgment action instituted by a patent licensee in good standing." *Gen-Probe*, 359 F.3d at 1382. That statement is a classic "distinction without a difference." The Federal Circuit failed to apply the principle on which the *Aetna* decision was based – the existence of a genuine dispute as to legal rights under a contract is sufficient to satisfy the case and controversy requirement – and instead dismissed the case because of immaterial factual differences. That error should be corrected in this case.

### *B. The Federal Circuit Fails to Follow this Court's Decision that the Public Interest is Best Served by Allowing Patent Licensees to Contest the Validity of the Licensed Patent.*

The Federal Circuit apparently believes that patent cases are categorically different from other contract disputes and thus not subject to the same standards for determining whether there is a federal case and controversy. The Circuit Court is wrong in that belief. Not only is there no valid analytical reason for a different rule in patent license cases, there is a strong public policy that supports application of the same principle applied to other types of commercial and contract disputes. That public policy is one that favors opening the judicial doors to issues of patent validity in order to protect the public interest from the adverse market consequences of invalid patents.

In *Lear v. Adkins* the Court reconsidered the estoppel doctrine that had developed in patent law and concluded that it was an unsound limitation. The Court had previously adopted a rule that estopped a licensee from attacking the validity of the patent in *Automatic Radio Manufacturing Co. v. Hazeltine Research, Inc.*, 339 U.S. 827 (1950). Upon reconsideration of that case, the Court held that it should be overruled. *Lear* rested on the realization that because patents have the effect of a limited monopoly, the public interest is better served by allowing licensees to contest the validity of the patent on which the license was based.

In *Gen-Probe*, the Federal Circuit, relying on a number of its own prior decisions, construed *Lear* narrowly and said that it "does not grant every licensee in every circumstance the right to challenge the validity of the patent." 359 F.3d at 1381. Here again the Federal Circuit failed to follow the principle that sustains the *Lear* precedent

and chose to follow its own precedent instead of this Court's controlling decision.

It is not clear why the Federal Circuit reached the result it did in *Gen-Probe* or in this case. Perhaps those decisions reflect an excessively rigid view of the general rule that decisions of a prior panel of the circuit control a subsequent panel – even if wrongly decided – until and unless overruled by the circuit sitting *en banc*. *See, e.g., Tate Access Floors, Inc. v. Interface Architectural Res., Inc.*, 279 F.3d 1357, 1366 (Fed. Cir. 2002) (panels of the Federal Circuit are bound by a prior panel ruling on the issue until and unless the prior decision is set aside by the court sitting *en banc*). Perhaps they reflect a pro-patent-validity policy of that court. Regardless of the reason, the rejection of *Lear* and *Aetna* by the circuit court was wrong then and remains wrong today. The Court should reject the narrow view of case and controversy jurisdiction that has been adopted by the Federal Circuit. The same public interest analysis applied to the issue of equitable estoppel in *Lear*, also applies in the context of case and controversy analysis. The analysis of equitable estoppel by this Court and the regional circuits shows that there is no constitutional issue that requires dismissal of declaratory judgment complaints filed by licensees.

## Conclusion

For the reasons stated, the Court should reverse the judgment of the Court of Appeals for the Federal Circuit.

Respectfully submitted,

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IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

v.

GENENTECH, INC., ET AL.,

*Respondents.*

On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

## BRIEF OF NATURAL RESOURCES DEFENSE COUNCIL, INC. AS AMICUS CURIAE IN SUPPORT OF PETITIONER

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## QUESTION PRESENTED

Does Article III's grant of jurisdiction of "all Cases ... arising under ... the Laws of the United States," implemented in the "actual controversy" requirement of the Declaratory Judgment Act, 28 U.S.C. § 2201(a), require a patent licensee to refuse to pay royalties and commit material breach of the license agreement before suing to declare the patent invalid, unenforceable, or not infringed?

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## INTEREST OF AMICUS CURIAE

The Natural Resources Defense Council, Inc. (NRDC) submits this brief as amicus curiae in support of the petitioner because affirmance of the Federal Circuit's decision would distort Article III's case-or-controversy requirement in ways that could have damaging effects on the justiciability of a broad range of cases not involving patents, including environmental litigation to which NRDC is often a party.[1]

NRDC is a nonprofit environmental membership organization founded in 1970. NRDC's purposes include protection of human health and the environment. NRDC's staff of lawyers, scientists, and other environmental professionals work to protect the planet's wildlife and wild places and to ensure safe and healthy communities for NRDC's more than one-half million members and their families.

NRDC's efforts to protect the environment often involve litigation. NRDC regularly seeks judicial review of governmental actions damaging to the environment, and it intervenes in cases where industry challenges government regulations and policies that protect the environment. *See, e.g., Chevron, U.S.A., Inc. v. NRDC*, 467 U.S. 837 (1984) (NRDC as plaintiff); *Orff v. United States*, 125 S. Ct. 2606 (2005) (NRDC as intervenor). NRDC also sues polluters directly in cases where federal or state law affords a right of action. *See, e.g., Gwaltney of Smithfield, Ltd. v. Chesapeake Bay Found.*, 484 U.S. 49 (1987); *NRDC v. Southwest Marine, Inc.*, 236 F.3d 985 (9th Cir. 2000).

Article III justiciability issues, particularly standing and ripeness, are often critically important in these cases. Indeed,

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[1] Letters of consent to the filing of this brief from all parties have been filed with the Clerk. This brief was not authored in whole or in part by counsel for a party. No person or entity other than amicus curiae, its members, or its counsel made a monetary contribution to the preparation or submission of this brief.

many of this Court's leading standing decisions have arisen from environmental litigation. *See, e.g., Sierra Club v. Morton*, 405 U.S. 727 (1972); *United States v. SCRAP*, 412 U.S. 669 (1973); *Duke Power Co. v. Carolina Envtl. Study Group, Inc.*, 438 U.S. 59 (1978); *Lujan v. Nat'l Wildlife Fed'n*, 497 U.S. 871 (1990); *Lujan v. Defenders of Wildlife*, 504 U.S. 555 (1992); *Bennett v. Spear*, 520 U.S. 154 (1997); *Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83 (1998); *Friends of the Earth, Inc. v. Laidlaw Envtl. Servs.*, 528 U.S. 167 (2000).

Although this case involves patent validity and not environmental issues, it implicates NRDC's interests because Article III's requirements apply to all cases, regardless of subject matter. A decision in a patent case that ignores or alters the criteria this Court has set forth for determining when an Article III case or controversy exists may affect all cases, including environmental litigation. NRDC is therefore keenly interested in the proper application of Article III's case-or-controversy requirement in this case.

## SUMMARY OF ARGUMENT

The Federal Circuit held in this case that there is no Article III case or controversy when a patent licensee sues a patent owner for a declaration of patent invalidity without first breaching the license agreement. In such a case, the court held, the licensee is "under no threat or apprehension of suit" and hence lacks "standing to bring a declaratory challenge." *MedImmune, Inc. v. Genentech, Inc.*, Nos. 04-1300, -1384, slip op. 9 (Fed. Cir. Oct. 18, 2005). In so holding, the lower court followed its previous decisions in *Gen-Probe, Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir. 2004), and *MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005), which similarly held that a licensee must breach its license agreement to create a justiciable case or controversy over the validity of the underlying patent.

Remarkably, in none of these opinions did the Federal Circuit so much as cite any of this Court's many recent

precedents defining when a plaintiff has standing to present a federal court with a case or controversy within the meaning of Article III. Those decisions establish that a plaintiff has standing, and that there is a justiciable case or controversy under Article III, when three elements are present: (1) the plaintiff has suffered or is likely to suffer a legally cognizable injury ("injury in fact"); (2) there is a fairly traceable causal relationship between the defendant's challenged conduct and the injury ("causation"); and (3) the relief sought from the defendant will likely redress the injury ("redressability"). *See, e.g., Vermont Agency of Natural Res. v. United States ex rel. Stevens,* 529 U.S. 765, 771 (2000).

Each of these elements, ignored by the Federal Circuit, is present here: The plaintiff has suffered a present and ongoing *injury* in having to pay money to the defendant to avoid a lawsuit for infringement; that injury was *caused by* the defendant's challenged conduct of obtaining an allegedly invalid patent; and a favorable decision on validity would likely *redress* the injury by relieving the plaintiff of the ongoing need to pay royalties to the defendant. Whatever obstacles there may be to the maintenance of this lawsuit, the absence of an Article III case or controversy is not one of them.

Moreover, the Federal Circuit's view that the existence of a case or controversy is negated by the plaintiff's choice of taking a costly action (paying royalties) to avoid an even more serious injury (being sued for damages for infringement, or possibly even treble damages and fees for willful infringement) could have far-reaching, negative consequences. Plaintiffs often choose a lesser form of injury over a greater one. For example, a plaintiff in an environmental case may choose to stop swimming in a river to avoid being harmed by pollutants, or a corporate plaintiff challenging a federal regulation may choose to bear the costs of complying with it rather than violate it and risk an enforcement action. The injury in such a case is no less real, and a case or controversy no less present, than in a case where the defendant has

no choice about how the injury will be suffered. Indeed, cases involving plaintiffs faced with the immediate dilemma of incurring costs of avoidance (or compliance) or suffering a direct injury are generally viewed as the *easiest* cases for justiciability purposes in that they readily satisfy not only Article III standing and ripeness requirements but also the additional prudential requirements of the ripeness doctrine. *See, e.g., Abbott Labs. v. Gardner*, 387 U.S. 136, 152-154 (1967).

Whether MedImmune's claim of patent invalidity is a justiciable case or controversy depends not on legal doctrines and policies exclusive to patent cases, but on the constitutional principles this Court has developed to implement the requirements of Article III, which are applicable to all federal judicial proceedings. Those principles, fairly applied, require the Court to reverse the Federal Circuit's holding that there is no Article III case or controversy here.

## ARGUMENT

### I. This Court Has Established That the Requisites of an Article III Case or Controversy Are Injury in Fact, Causation, and Redressability.

Article III, section 2 extends the judicial power of the United States only to "cases" and "controversies." The Declaratory Judgment Act, 28 U.S.C. § 2201, which MedImmune has invoked in this case, similarly empowers federal courts to provide declaratory remedies only in "case[s] of actual controversy within [their] jurisdiction," a phrase that incorporates the same limitations as the constitutional provision. *See, e.g., Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 239-240 (1937); *Ashwander v. TVA*, 297 U.S. 288, 325 (1936).

The case-or-controversy requirement embodies a number of "doctrines that cluster about Article III—not only standing but mootness, ripeness, political question, and the like," *Allen v. Wright*, 468 U.S. 737, 750 (1984) (citation omitted), all designed to limit courts to their "proper—and properly lim-

ited—role ... in a democratic society." *Warth v. Seldin*, 422 U.S. 490, 498 (1975). Among the critical functions served by the case-or-controversy requirement is limiting intervention by the courts to disputes that are sufficiently "concrete" (as opposed to merely "abstract") to entitle the parties to judicial resolution. *Allen*, 468 U.S. at 750-52.

Of the doctrines devised by the courts to achieve this objective, standing "is perhaps the most important." *Id.* at 750. Over the past quarter century, this Court has repeatedly addressed the requirements of standing and refined them into a now-familiar litany: "[T]he 'case' or 'controversy' provision of Article III" requires, as an "'irreducible constitutional minimum' ... (1) that the plaintiff have suffered an 'injury in fact'—an invasion of a judicially cognizable interest which is (a) concrete and particularized and (b) actual or imminent, not conjectural or hypothetical; (2) that there be a causal connection between the injury and the conduct complained of—the injury must be fairly traceable to the challenged action of the defendant, and not the result of the independent action of some third party not before the court; and (3) that it be likely, as opposed to merely speculative, that the injury will be redressed by a favorable decision." *Bennett v. Spear*, 520 U.S. at 167. The Court has emphasized over and over that the three critical elements of injury in fact, causation, and redressability are the *sine qua non* of standing under Article III. *See, e.g., McConnell v. FEC*, 540 U.S. 93, 225 (2003); *Stevens*, 529 U.S. at 771; *Laidlaw*, 528 U.S. at 180-81; *Lujan v. Defenders of Wildlife*, 504 U.S. at 560-61; *Lewis v. Cont'l Bank Corp.*, 494 U.S. 472, 477 (1990); *Valley Forge Christian College v. Americans United for Separation of Church and State*, 454 U.S. 464, 472 (1982).[2]

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[2] The other two principal elements of the case-or-controversy requirement, ripeness and mootness, which are not at issue here, address the interaction of the standing requirements with matters of timing, but do not add new elements to the basic building blocks of a case or controversy.

(*Footnote continued*)

## II. The Federal Circuit's Holding That MedImmune's Claim Presents No Case or Controversy Cannot Be Squared with this Court's Article III Case Law.

Although it held that MedImmune's claims do not present an Article III case or controversy, the Federal Circuit did not attempt to analyze whether those claims satisfied the "irreducible constitutional minimum" requirements of standing (*Bennett*, 520 U.S. at 162) as set forth in this Court's decisions. Indeed, neither in the opinion below nor in its predecessors, *Gen-Probe*, 359 F.3d 1376, and *MedImmune v. Centocor*, 409 F.3d 1376, did the Federal Circuit even relate its Article III holding to this Court's many recent precedents defining the bounds of the case-or-controversy requirement.[3]

A straightforward application of this Court's precedents to MedImmune's claims demonstrates that there is a case or controversy here. MedImmune claims that, to avoid liability for infringing Genentech's patent, it has paid substantial royalties to Genentech. The monetary losses MedImmune has thus sustained constitute the quintessential injury in fact; it is uncontroversial that "[p]ecuniary injury is a sufficient basis for standing." *Fair v. EPA*, 795 F.2d 851, 853 (9th Cir.

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The constitutional dimension of ripeness, for example, is satisfied at least where the plaintiff's injury is imminent enough to confer standing, *see NTEU v. United States*, 101 F.3d 1423, 1427-28 (D.C. Cir. 1996), and the mootness doctrine demands *less* concreteness than is necessary for standing at the commencement of litigation. *See Laidlaw*, 528 U.S. at 190-92.

[3] There is no doubt that the Federal Circuit's holdings rested on Article III. Although the term "standing" is also used to refer to prudential, non-constitutional limits on justiciability, and sometimes to denote whether a plaintiff has satisfied the requirements necessary to bring a particular cause of action (for example, "antitrust standing"), each of the Federal Circuit's opinions expressly stated that what was lacking, in the court's view, was an Article III case or controversy. *See MedImmune v. Genentech*, slip op. at 5; *MedImmune v. Centocor*, 409 F.3d at 1378-79, 1382; *Gen-Probe*, 359 F.3d at 1379. This Court, in turn, granted certiorari solely to determine the scope of "Article III's grant of jurisdiction."

1986). *See, e.g., Bacchus Imports, Ltd. v. Dias*, 468 U.S. 263, 267 (1984); *Gen. Motors Corp. v. Tracy*, 519 U.S. 278, 286 (1997); *Barlow v. Collins*, 397 U.S. 159, 163-64 (1970). The injury satisfies the causation element of standing because it is "fairly traceable" to Genentech's procurement of an allegedly invalid patent and its efforts to license or enforce the patent. Absent the patent, MedImmune would not have to pay Genentech royalties for the use of the invention. And the injury is redressable through the relief MedImmune seeks, for it is at least likely that a declaration that the patent is invalid will effectively relieve MedImmune from the obligation to pay royalties by providing it a defense against an effort by Genentech to enforce the license agreement. *See Lear, Inc. v. Adkins*, 395 U.S. 653 (1969).

That the application of this Court's Article III precedents leads to this result should come as no surprise, because this Court long ago held that the payment of royalties to avoid infringement of an allegedly invalid patent creates a case or controversy. In *Altvater v. Freeman*, 319 U.S. 359, 365 (1943), this Court held that "the requirements of case or controversy are met where payment of a claim is demanded as of right and where payment is made, but where the involuntary or coercive nature of the exaction preserves the right to recover the sums paid or to challenge the legality of the claim." Indeed, this passage from *Altvater* anticipates all the elements of this Court's later-articulated standing analysis and demonstrates how each one is satisfied: (1) injury ("payment is made"); (2) causation (payment is "demanded as of right" and is "involuntary or coercive"); and (3) redressability (there is a right to "recover the sums paid or to challenge the legality of the claim").

## III. The Federal Circuit's Reasoning, If Applied in Other Settings, Would Radically Alter Conventional Justiciability Analysis.

The Federal Circuit nonetheless held that there is no case or controversy here simply because the plaintiff is "under no

threat or apprehension of suit." *MedImmune v. Genentech*, slip op. 9. This statement is perplexing, and, from the standpoint of this Court's Article III jurisprudence, a non sequitur. Whether a plaintiff has Article III standing to bring a declaratory judgment action depends on whether it has suffered injury, caused by another's allegedly wrongful conduct, that can be redressed by a declaratory judgment, not on whether the *defendant* has a cause of action against the *plaintiff*.

Moreover, to the extent the Federal Circuit's analysis suggests that making payments or taking other volitional actions to avoid a more serious injury (here, being sued for infringement) does not constitute an injury, the court's holding is flatly inconsistent with conventional standing principles that are routinely applied in other types of cases.

For example, the injury in fact suffered by plaintiffs in environmental cases often consists of actions they choose to take to minimize their exposure to health threats posed by environmental contamination. In this Court's decision in *Laidlaw*, the injury on which this Court's recognition of the plaintiff's standing rested was that the plaintiff organization had members who had curtailed their use of the North Tyger River because of the defendant's discharge of pollutants into it. That is, the organization's members had chosen not to fish or swim in the river, to canoe on it, or to hike, camp, or picnic near it, in order to avoid exposure to noxious and hazardous pollutants. 528 U.S. at 181-83. Similarly, lower courts regularly recognize that environmental plaintiffs who have stopped engaging in recreational activities in polluted areas have suffered injuries sufficient to support standing. *See, e.g., American Canoe Ass'n, Inc. v. City of Louisa Water & Sewer Comm'n*, 389 F.3d 536 (6th Cir. 2004), *American Canoe Ass'n v. Murphy Farms, Inc.*, 326 F.3d 505 (4th Cir. 2003); *Piney Run Pres. Ass'n v. County Comm'rs*, 268 F.3d 255 (4th Cir. 2001); *Ecological Rights Found. v. Pacific Lumber Co.*, 230 F.3d 1141 (9th Cir. 2000), *Friends of the Earth, Inc. v. Gaston Copper Recycling Corp.*, 204 F.3d 149 (4th Cir.

2000). If the Federal Circuit were to prevail in its view that such avoidance injuries do not suffice to create a case or controversy, plaintiffs in such cases could not gain access to court without eating contaminated fish or swimming in sewage.

Similarly, plaintiffs in First Amendment cases suffer injury in fact not only when the government takes action against them for engaging in protected speech, but also when they change their behavior to avoid a genuine threat of such direct consequences. Thus, this Court found a justiciable controversy in *Steffel v. Thompson*, 415 U.S. 452 (1974), where the plaintiff alleged that he had decided to stop distributing handbills at a shopping mall in order to avoid prosecution. As the Court explained, "it is not necessary that petitioner first expose himself to actual arrest or prosecution to be entitled to challenge a statute that he claims deters the exercise of his constitutional rights." *Id.* at 459. And the Court held in *Meese v. Keene*, 481 U.S. 465, 472-73 (1987), that a plaintiff suffered injury in fact when he chose not to show films branded as propaganda by the government in order to avoid the reputational injuries that would follow if he were associated with such propaganda.

Lower courts also regularly hold that plaintiffs who change their conduct in order to avoid a realistic threat of sanctions have standing to raise First Amendment challenges to the laws that pose the threat. *E.g., Eldred v. Reno*, 239 F.3d 372, 375 (D.C. Cir. 2001) (plaintiffs had standing to challenge copyright statute because they were injured by *compliance* with its restrictions on exploitation of copyrighted works), *aff'd sub nom. Eldred v. Ashcroft*, 537 U.S. 186 (2003); *see also Brister v. Faulkner*, 214 F.3d 675, 679-81 (5th Cir. 2000); *Wilson v. State Bar*, 132 F.3d 1422, 1428 (11th Cir. 1998); *Jacobs v. Florida Bar*, 50 F.3d 901, 904-05 (11th Cir. 1995); *Int'l Soc'y for Krishna Consciousness v. Eaves*, 601 F.2d 809, 817-19 (5th Cir. 1979). As the First Circuit has put it, a threat of sanctions if a plaintiff exercises

First Amendment rights "poses a classic dilemma for an affected party: either to engage in the expressive activity, thus courting prosecution, or to succumb to the threat, thus forgoing free expression. Either injury is justiciable." *New Hampshire Right to Life Political Action Comm. v. Gardner*, 99 F.3d 8, 14 (1st Cir. 1996). The Federal Circuit's justiciability analysis is difficult, if not impossible, to square with this firmly established precedent.

The Federal Circuit's view would be equally devastating to corporate plaintiffs seeking to challenge government regulations that they claim go too far. Plaintiffs in such cases typically are not required to take the risk of *violating* a regulation in order to challenge it. Rather, they rely on costs of *compliance* (similar to the costs MedImmune has incurred to comply with its license terms) to establish their injury for standing purposes. *See, e.g., City of Waukesha v. EPA*, 320 F.3d 228, 234 (D.C. Cir. 2003) ("The administrative record shows that the City of Waukesha would face substantial costs if it was required to comply with the [challenged] regulations. This is sufficient for injury-in-fact."); *Cellco P'ship v. FCC*, 357 F.3d 88, 100 (D.C. Cir. 2004) ("As an entity continuously burdened by the costs of complying ... with what it contends are 'unnecessary' regulations ..., Verizon Wireless' injuries are concrete and actual, traceable to the Commission's alleged failure to meet the statutory deadline, and redressable by a ruling adopting Verizon Wireless' interpretation [of the statute]."); *Ass'n of Am. R.Rs. v. Department of Transp.*, 38 F.3d 582, 585-86 (D.C. Cir. 1994) (cost of compliance with two sets of regulations sufficient to support standing). Under the Federal Circuit's view of standing, industry plaintiffs in these and similar cases would have to violate applicable regulations and put themselves at risk of being sued (or possibly even criminally prosecuted) by the government before they could present the courts with a justiciable controversy.

That would constitute a significant reversal of ordinary notions of justiciability in administrative law cases. Indeed, cases where a plaintiff faces the dilemma of either taking costly measures to comply with a regulation or violating it and facing an enforcement action are generally considered the easiest from the standpoint of justiciability, because they most readily satisfy not only the constitutional case-or-controversy requirement, but also prudential limitations on ripeness. *See, e.g., Abbott Labs.*, 387 U.S. at 152-154 (holding a controversy was ripe where the plaintiff either had to incur compliance costs or risk prosecution); *Nat'l Ass'n of Home Builders v. United States Army Corps of Eng'rs*, 417 F.3d 1272, 1284 (D.C. Cir. 2005) (holding a claim justiciable where the plaintiffs were required "either [to] modify their projects to conform to [required] thresholds and conditions ... or refrain from building until they can secure individual permits"); *Ciba-Geigy Corp. v. EPA*, 801 F.2d 430 (D.C. Cir. 1986) (holding a claim justiciable where "[t]he Company's only alternative to costly compliance with EPA's regulatory directive would be to run the risk of serious civil and criminal penalties"). By ruling that there is no case or controversy in precisely analogous circumstances, the Federal Circuit has turned ordinary justiciability principles upside down.

## IV. This Case Does Not Turn on Legal Principles or Policies Unique to Patent Litigation.

Article III applies equally to all cases in the federal courts, and its basic requirements generally do not vary with the subject matter of the case. The Federal Circuit held not that patent cases require prudential limitations on standing or that there is no right of action in cases such as this one, but that this case involves no Article III case or controversy. That holding—which is the only one before this Court—turns on "general principles of law with which [this Court is] familiar," not on "the peculiarities of patent litigation." *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 103 (1993) (Scalia, J., concurring in part and in the judgment). In *Cardi-*

*nal Chemical*, for example, the majority applied general Article III principles to hold that an appellate ruling of noninfringement does not moot the issue of patent validity if there was a live controversy over validity in the trial court. The Court then went on to consider policies specific to patent litigation in determining whether there was a valid *nonconstitutional* basis for the Federal Circuit's practice of vacating declaratory judgments on validity when it held that a patent was not infringed. *See* 508 U.S. at 96-103.

In this case, the question on which the Court granted certiorari is limited to the constitutional issue, so there is no reason to proceed further once that issue is resolved. The Federal Circuit's apparent view that permitting suits in the circumstances here is not sound policy because it leads to some "inequity" or "imbalance" between patent owners and licensees (*MedImmune v. Genentech*, slip op. 7), even if it were convincing, is irrelevant to the issue before the Court. That issue is no more and no less than whether such disputes present an Article III case or controversy.[4]

The Federal Circuit seems to have gone astray by confusing the case-or-controversy issue with the question whether a licensee has a *right of action* in these circumstances. That could well be a more difficult question, and one to which policies and legal principles specific to patent cases would be relevant. Whatever the answer to that question might be, its resolution, unlike the resolution of the case-or-controversy issue, would not have the potential to distort time-honored,

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[4] The Federal Circuit's view that it is somehow inequitable to permit a challenge to a patent without requiring the challenger to infringe it is, in any event, hard to square with the fact that one of the principal purposes of the Declaratory Judgment Act was to relieve parties of the "*in terrorem* choice" between engaging in conduct that may subject them to suit or giving in to the threat posed by a patent owner or other potential plaintiff who seeks to coerce them into complying with its wishes. *See Cardinal Chem. Co.*, 508 U.S. at 95-96.

generally applicable Article III principles and settled policies regarding the justiciability of a wide range of cases involving federal statutes and regulations outside the patent field.

The cause-of-action question might be difficult in part because the Declaratory Judgment Act, 28 U.S.C. § 2201, has been held not to create new causes of action, but only to provide a form of relief that may be granted in otherwise cognizable cases. *See Skelly Oil Co. v. Phillips Petroleum Co.*, 339 U.S. 667 (1950). The form of relief made available by the Act often permits a suit to be initiated by the party who would normally be the defendant in a coercive action, but according to the *Skelly* doctrine it does not alter the elements of the underlying cause of action that must be set forth in a well-pleaded complaint, nor does it transform *defenses* into elements of affirmative causes of action. *See id.* Because patent invalidity is primarily a defense (either to a claim of patent infringement under 35 U.S.C. § 281, which presents a federal question, or to a contractual claim of breach of a license agreement, which does not, *see Milprint, Inc. v. Curwood, Inc.*, 562 F.2d 418 (7th Cir. 1977)), it is conceivable that there would be no *cause of action* for a declaratory judgment of invalidity when the patent owner would have no cause of action for infringement or breach of a license agreement. Of course, a party seeking to argue that there would be no cause of action in such circumstances would have to account for this Court's statement in *Cardinal Chemical* that "a party seeking a declaratory judgment of invalidity presents a claim independent of the patentee's charge of infringement." 508 U.S. at 96.

Whether there is a cause of action (an issue on which we take no position here) is, however, a question wholly distinct from the antecedent question whether there is an Article III case or controversy. *See Steel Co.*, 523 U.S. at 89 ("[T]he absence of a valid (as opposed to arguable) cause of action does not implicate subject-matter jurisdiction, i.e., the courts' statutory or constitutional power to adjudicate the case."); *see*

*also Arbaugh v. Y & H Corp.*, 126 S. Ct. 1235, 1242-44 & n.10 (2006). Only the latter question is presented by this case, and the Federal Circuit's answer to that question cannot be squared with this Court's consistent and longstanding construction of the requirements of Article III.

## CONCLUSION

For the foregoing reasons, the judgment of the Federal Circuit should be reversed.

Respectfully submitted,

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IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner*,

*v.*

GENENTECH, INC., *et al.*,

*Respondents.*

ON WRIT OF CERTIORARI TO THE
UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

## BRIEF OF NEW YORK INTELLECTUAL PROPERTY LAW ASSOCIATION AS *AMICUS CURIAE* IN SUPPORT OF RESPONDENTS

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## STATEMENT OF INTEREST OF AMICUS CURIAE

This brief amicus curiae is submitted in support of Respondents by the New York Intellectual Property Law Association (the "NYIPLA" or the "Association"), a professional association of more than 1,300 attorneys whose interests and practices lie in the area of patent, copyright, trademark, trade secret and other intellectual property law.[1]

NYIPLA members include in-house attorneys working for businesses that own, enforce and challenge patents as well as attorneys in private practice who represent both patent owners and accused infringers. NYIPLA members frequently engage in patent licensing matters, representing both patent licensors and licensees.

NYIPLA members represent both plaintiffs and defendants in infringement litigation and also regularly participate in proceedings before the United States Patent and Trademark Office ("PTO"), including representation of applicants for patents and parties to interferences. A substantial percentage of NYIPLA members participate actively in patent litigation. Many NYIPLA members engaged in patent litigation also negotiate patent licenses in the context of settlement.

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1. Pursuant to SUP. CT. R. 37.6, the NYIPLA and its counsel represent that they have authored this brief in whole, and that no person or entity other than the amicus curiae and its counsel have made a monetary contribution to the preparation or submission of this brief. Pursuant to SUP. CT. R. 37.3, both petitioner and respondents have consented to the filing of this brief.

## QUESTION PRESENTED

Does Article III's grant of jurisdiction of "all Cases . . . arising under . . . the Laws of the United States," implemented in the "actual controversy" requirement of the Declaratory Judgment Act, 28 U.S.C. § 2201(a), require a patent licensee to refuse to pay royalties and commit material breach of the license agreement before suing to declare the patent invalid, unenforceable or not infringed?

## POSITION OF AMICUS REGARDING QUESTION PRESENTED

The Association respectfully submits that a patent licensee in full compliance with its license obligations should not be permitted to sue so as to declare the licensed patent invalid, unenforceable or not infringed.

## SUMMARY OF ARGUMENT

A patent licensee should not be permitted to wield the sword of patent challenge while at the same time using the license as a shield against infringement liability and the risk of an injunction. A patentee should not be required to grant an unconditional waiver of its right to sue for infringement if the licensee can challenge a licensed patent without consequence.

As discussed in Part I, Respondents' inability to sue Petitioner for patent infringement and the absolute lack of risk of future litigation against Petitioner as long as it maintains good standing under the license mandate that there is no actual controversy here under principles of mutuality.

As discussed in Part II, no extension of *Lear v. Adkins* is warranted because of subsequent changes in statutory provisions and case law.

Finally, as discussed in Part III, if a licensee in good standing were allowed to maintain litigation by attacking a licensed patent, perverse incentives and a moral hazard would be created whereby: (1) patentees would be less likely to grant licenses because the patentee would be in a worse position for having granted a license; and (2) an accused infringer would have strong incentive to enter into a sham license and then proceed from the bargaining table to the courthouse.

## ARGUMENT

### I. PETITIONER'S ARGUMENT CONTRAVENES THE REQUIREMENT OF MUTUALITY SET FORTH IN *AETNA LIFE INSURANCE CO. v. HAWORTH.*

Petitioner cannot be sued so long as it complies with its licer e obligations. Accordingly, no justiciable controversy exists because Respondents are barred from suing Petitioner in a suit for patent infringement or breach of contract. For justiciability, "[i]t is the nature of the controversy, *not the method of its presentation or the particular party who presents it*, that is determinative." *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 244 (U.S. 1937) (emphasis added). But if this action were to go forward, justiciability *would* depend on the method of its presentation or the particular party who presented it: only Petitioner could bring it.

The existence of an "actual controversy" under the Declaratory Judgment Act is based on the totality of the circumstances.

> Basically, the question in each case is whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.

*Maryland Casualty Co. v. Pac. Coal & Oil Co.*, 312 U.S. 270, 273 (1941).

An actual controversy requires mutuality, at least potentially. Justiciability attaches to the controversy and not to the party that presents it. *Aetna Life Ins.*, 300 U.S. at 244. A party need not immediately be exposed to liability, but there must at least be the potential for liability in the reasonably foreseeable future. *Maryland Casualty*, 312 U.S. at 273 (likely future liability of insurer against party injured by insured). In the patent context, the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit") has fairly synthesized these principles into a rule that an actual controversy exists when there is "a reasonable apprehension on the part of the declaratory judgment plaintiff that it will face an infringement suit".[2] *MedImmune, Inc. v. Genentech*,

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2. This rule also is a legal standard guiding discretion to hear patent declaratory judgment actions. "[C]onsiderations of practicality and wise judicial administration" permit courts to refuse to take jurisdiction over declaratory judgment actions *Wilton v. Seven Falls Co.*, 515 U.S. 277, 288 (U.S. 1995). Ordinarily, "the fitness of the case for resolution, are peculiarly within the[] grasp [of the district (Cont'd)

*Inc.*, 427 F.3d 958, 964 (Fed. Cir. 2005); *see also MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376 (Fed. Cir. 2005); *BP Chems. Ltd. v. Union Carbide Corp.*, 4 F.3d 975, 977-78 (Fed. Cir. 1993) (synthesis of rule).

*Maryland Casualty* is a good example of mutuality. An actual controversy existed between an insurer and a party injured in an automobile accident with the insured, but before the insured's liability had been established. *Maryland Casualty*, 312 U.S. at 271-72. In every real sense, because of the insurance relationship, the insurer was a party to the ongoing controversy between the insured and injured party — "the potential or prospective claim of the injured person against the insurance company makes him a proper, if not indeed a necessary party defendant in a suit by the insurance company against the insured for a declaration of non-liability." EDWIN BORCHARD, DECLARATORY JUDGMENTS 42 (2d ed. 1941). The insurer was presently obliged to defend the insured and to indemnify the insured, if the accident was within the scope of the coverage. *Maryland Casualty*, 312 U.S. at 271. The insurer also was basically a stakeholder potentially subject to inconsistent judgments from suit by the insured and injured party. *Id.* at 274.

Mutuality of controversy is consistent with the historical background of the Declaratory Judgment Act. Before the Act, patentees, in particular, enjoyed "[u]nfair [p]rivileges".

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(Cont'd)

courts]." *Id.* at 289. But "[d]iscretion is not whim, and limiting discretion according to legal standards helps promote the basic principle of justice that like cases should be decided alike." *Martin v. Franklin Capital Corp.*, 126 S. Ct. 704, 710 (2005). Patentees, licensees, and accused infringers should have clear rules regarding justiciability.

BORCHARD at 803. Only a patentee could instigate litigation that could conclusively establish the infringement, validity or enforceability of a patent. The accused infringer was powerless to compel litigation via a declaratory judgment action, even when threatened. *Id.* The Act put the patentee and an accused infringer on equal footing – an accused infringer could now compel litigation when actually accused of infringing a patent and litigate the defenses of invalidity, noninfringement and unenforceability.

Declaratory judgment actions often are "inverted" – "the plaintiff seeking the declaratory judgment is . . . the party who would be the defendant in a coercive suit for damages or an injunction." *Gator.com Corp. v. L.L. Bean, Inc.*, 398 F.3d 1125, 1137 (9th Cir. 2005) (Feltcher, J., dissenting); *see also Beacon Theatres, Inc. v. Westover*, 359 U.S. 500, 504 (U.S. 1959). Inverted actions allow defenses to be raised as affirmative actions. *See Public Service Comm'n. v. Wycoff Co.*, 344 U.S. 237, 248 (U.S. 1952). "It is immaterial that frequently, in the declaratory judgment suit, the positions of the parties in the conventional suit are reversed; *the inquiry is the same in either case*." *Maryland Casualty*, 312 U.S. at 273 (emphasis added).

Here, Petitioner's action is an inverted patent infringement or contract enforcement action in which patent defenses would be raised affirmatively. Invalidity, unenforceability and noninfringement are specifically enumerated patent defenses under 35 U.S.C. § 282.

Petitioner's action is not analogous to a declaration construing the scope of a contract. Each of the issues to be litigated is an explicit statutory patent infringement defense, and the patent law, in turn, makes them defenses to patent

license enforcement. *See, e.g., Lear, Inc. v. Adkins*, 395 U.S. 653 (1969) (invalidity of licensed patent is a defense to the enforcement of license). While the issues can formally be phrased as construction of a contract — through construction of the underlying patent — that results in putting form over substance.

Formation of the precise inverted suit is difficult. Absent a license, an accused infringer's declaratory judgment action for patent invalidity is an inverted patent infringement action in which the affirmative defense of invalidity would be pleaded. *See In re Lockwood*, 50 F.3d 966, 974 (Fed. Cir. 1995), *cert. granted sub nom. Am. Airlines v. Lockwood*, 515 U.S. 1121 (1995), *cert. dismissed, vacated as moot*, 515 U.S. 1182 (1995) (jury trial request withdrawn); *see also id.* at 975 n.11.

But both a patent and a license are involved. A patent license is a contract that is "a mere waiver of the right to sue by the patentee" for infringement. *De Forest Radio Tel. Co. v. United States*, 273 U.S. 236, 242 (U.S. 1927) (quoting *Henry v. A.B. Dick Co.*, 224 U.S. 1 (1911)). A license also is an authorization that makes certain uses of an invention constitute noninfringement. 35 U.S.C. §§ 271(a) and (g). Thus, a license is a "complete defense against a suit for infringement." *De Forest*, 273 U.S. at 242. Violation of a license, however, is cognizable *both* as patent infringement *and* a breach of the license. *Gen. Talking Pictures Corp. v. West. Elec. Co.*, 304 U.S. 175, 181-82 (U.S. 1938). A patentee may, *at its choice*, sue for breach of contract or infringement, or both, following a breach. *Id.*

A declaratory judgment action initiated by a breaching licensee can be characterized as an inverted breach of a patent

or a contract action, or perhaps both, in which patent defenses are pleaded.[3]

However, Petitioner has not materially breached the license, making Petitioner's suit ambiguous. Petitioner is immune from suit for both patent infringement and breach of contract because the patentee has waived that right, so long as there is no material breach. Clearly, no action lies for breach. Respondents are absolutely barred from suing, so long as the licensee continues to pay royalties and otherwise complies with the license. *See De Forest Radio,*

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3. The ambiguous nature of this suit may raise an appellate subject matter jurisdiction issue. A patentee's choice of theories in a coercive action determines whether the action arises under the patent laws. 28 U.S.C. § 1338(a); *Christianson v. Colt Indus. Operating Corp.*, 486 U.S. 800, 808 (1988); *see also Holmes Group, Inc. v. Vornado Air Circulation Sys., Inc.*, 535 U.S. 826 (2002). Jurisdiction in an inverted declaratory judgment action is based on a hypothetical affirmative action, not the defense to be litigated. *Public Service Comm'n. v. Wycoff Co.*, 344 U.S. 237, 248 (U.S. 1952). A breach of patent license action does not arise under the patent laws, even if patent defenses are raised.. *See, e.g., Lear, Inc. v. Adkins*, 395 U.S. 653 (1969) (state court license action); *Farmland Irrigation Co. v. Dopplmaier*, 48 Cal. 2d 208, 217 (Cal. 1957). Under Federal Circuit law, a licensee's declaratory action challenging a licensed patent arises under the patent laws thus resulting in Federal Circuit appellate jurisdiction, *C.R. Bard, Inc. v. Schwartz*, 716 F.2d 874, 878-80 (Fed. Cir. 1983), but other Circuits have held that these actions sound in contract and *do not* arise under the patent laws, *Id; see, e.g., Thiokol Chem. Corp. v. Burlington Indus., Inc.*, 448 F.2d 1328, 1330-31 (3d Cir. 1971); *Prod. Eng'g & Mfg., Inc. v. Barnes*, 424 F.2d 42, 44 (10th Cir. 1970). *C.R. Bard* may be inconsistent with *Christianson* and *Holmes Group*. In this case, aside from the declaratory judgment action, "no other claims in MedImmune's complaint 'arise under' patent law." *MedImmune, Inc. v. Genentech, Inc.*, 427 F.3d 958, 971 (Fed. Cir. 2005) (Clevenger, J. dissenting).

273 U.S. at 242 (sustaining demurrer and dismissing petition seeking infringement damages because accused infringer had a license).

Finally, Respondents are estopped from terminating a license while a licensee complies with its license obligations. *See MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376, 1381 (Fed. Cir. 2005). Consequently, there is not even *risk* of future liability on Petitioner's part so long as it continues to comply with its license obligations.

Permitting this suit to go forward would contravene the mutuality required under *Aetna Life* and *Maryland Casualty*. The justiciability of the claim would depend on the party presenting it: Petitioner, and *only* Petitioner, could force judicial resolution of this ostensible controversy. Consequently, there is no "actual controversy."

*Altvater v. Freeman* does not mandate a different result. *Altvater v. Freeman*, 319 U.S. 359 (1943). The issue in *Altvater* was mootness, not, as here, whether there was a justiciable controversy in the first instance. A declaratory judgment of patent invalidity was brought as a counterclaim after the licensee already had been sued for specific performance of the license, an accounting and an injunction regarding (allegedly) licensed reissued patents. *Id.* at 360. The licensee counterclaimed for a declaratory judgment that the patent was invalid, or, if valid, that the license covered their actions. The Circuit Court of Appeals eventually held the invalidity counterclaims became moot based on the district court finding noninfringement and the contract having been terminated. *Id.* at 362-63. This Court held that "the issues raised by the present counterclaim were justiciable and did not come to an end . . . on the dismissal of the bill

for non-infringement. . . ." *Id.* at 363-64. Ultimately, "the issues raised by the counterclaim . . . were not . . . moot." *Id.* at 365.

The fact that the patentee-licensor originally sued the licensee for breach of the license, the equivalent of infringement of the patent, is critical. The act of suing created a mutual controversy sufficient to support the licensee's declaratory judgment counterclaims over the whole patent, not just the particular claims the patentee wished to litigate. Once "a party has actually been charged with infringement of the patent, there is, *necessarily*, a case or controversy adequate to support jurisdiction of a complaint, or a counterclaim, under the [Declaratory Judgment] Act." *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 96 (U.S. 1993). The royalties in *Altvater* were irrelevant. The licensee could have accordingly been liable for infringement or breach.

## II. *LEAR* SHOULD NOT BE EXTENDED TO PERMIT PATENT CHALLENGES BY A LICENSEE WHO CONTINUES TO PAY ROYALTIES.

*Lear v. Adkins* does not give a licensee a right to challenge a licensed patent while continuing to pay royalties. *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969). *Lear* "permits an accused infringer to accept a license, pay royalties for a time, and cease paying when financially able to litigate validity, secure in the knowledge that invalidity may be urged when the patentee-licensor sues for unpaid royalties." *Blonder-Tongue Labs., Inc. v. Univ. of Ill. Fdn.*, 402 U.S. 313, 346 (1971). That is, *Lear* permits a licensee to raise invalidity as a *defense* when sued after ceasing to pay royalties, and by extension, in an inverted declaratory judgment action – just

as the law presently allows. *Cf. Cordis Corp. v. Medtronic, Inc.*, 780 F.2d 991, 995 (Fed. Cir. 1985) (*Lear* "permit[s] a licensee to cease payments due under a contract while challenging the validity of a patent. It does not permit the licensees to avoid facing the consequences that such an action would bring.").

*Lear* was undoubtedly correctly decided, but more recent decision of this Court along with statutory changes militate against extending a licensee's right to challenge a patent while continuing to pay royalties. *Lear* reasoned, in part, that a licensee should not "pay tribute to would-be monopolists" and that "the *ex parte* nature of the prosecution proceeding is inherently suspect." *Lear*, 395 U.S. at 670.

This Court recently held that a patent does not create a presumption that a patentee has market power over the covered products and, therefore, that patentees are not truly "would be monopolists." *Ill. Tool Works, Inc. v. Indep. Ink, Inc.*, 126 S. Ct. 1281, 1284 (2006). In addition, although a "policy of free competition runs deep in our law", "the policy of stimulating invention that underlies the entire patent system runs no less deep." *Dawson Chem. Co. v. Rohm & Haas Co.*, 448 U.S. 176, 221 (1980). A patentee also is free to enforce its patent rights without fear of antitrust liability so long as its infringement claim is not subjectively and objectively baseless. *See Prof'l Real Estate Investors, Inc. v. Columbia Pictures Indus., Inc.*, 508 U.S. 49, 60 (1993).

As for the *ex parte* prosecution system, changes to the Patent Statute enacted by Congress have made it possible for licensees to challenge patents without having to engage in direct litigation with the patentee. At the time of *Lear*, the only way a private party could challenge an issued patent

was through litigation between itself and the patentee. A licensee may now rely on the preclusive effect of an invalidated patent in litigation with another party. *Blonder-Tongue*, 402 U.S. at 346-47.

Moreover, in 1980, Congress created the reexamination process, which allows PTO review of issued patents for substantial new questions of patentability and can be initiated by a private party's submission of prior art not considered in the original prosecution. P.L. 96-517 (1980), codified as amended at 35 U.S.C. §§ 301-307 (2000 & Supp. III 2003) (*ex parte*); *see also* P.L. 106-113 (1999) (creating *inter partes* reexamination), codified as amended at 35 U.S.C. §§ 311-318; P.L. 107-273 (2002) (expanding the scope of reexamination). Thus, while licensees needed access to the courts to challenge licensed patents at the time of *Lear*, today's licensees are not so limited. In fact, the patent involved in this case is presently in reexamination. Pet. Br. at 48 n. 18. Finally, the decisions of the PTO, an administrative agency, are now due even greater deference than they were at the time of *Lear*. *See, e.g.*, *Dickinson v. Zurko*, 527 U.S. 150 (1999).

## III. PETITIONER'S PROPOSED CHANGE WOULD CREATE NEEDLESS LITIGATION AND REDUCE THE LIKELIHOOD THAT PATENT DISPUTES CAN BE SETTLED BY LICENSING.

Patent licenses serve two important functions: (1) they encourage the development and commercialization of inventions; and (2) they allow settlement of patent litigation. The change in the law proposed by Petitioner would decrease a patentee's incentive to license and would therefore discourage commercialization and encourage wasteful litigation.

Patent licensing is generally economically efficient and procompetitive. *See* U.S. DEP'T OF JUSTICE & FTC, ANTITRUST GUIDELINES FOR THE LICENSING OF INTELLECTUAL PROPERTY 2 (1995), *reprinted in* 4 Trade Reg. Rep. (CCH) ¶ 13,132 (1995), ("intellectual property licensing allows firms to combine complementary factors of production and is generally procompetitive."). But licensing is voluntary on the patentee's part[4], so creating sufficient incentives for patentees to license their inventions is important.

Commercialization of inventions often relies on licensing. Many times, patentees are unable to bring their product to market alone and, therefore, rely on a licensee to do so. Also, the potential for licensing revenue is what drives many inventors to invent.

Congress encourages the licensing of patented inventions developed with federal funds because it encourages invention and commercialization of the inventions. "It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions . . . [including] to promote the commercialization and public availability of inventions made in the United States by United States industry and labor." 35 U.S.C. § 200. The Bayh-Dole Act, 35 U.S.C. §§ 200-212, "enables universities to profit from their federally-funded research." *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 929 (Fed. Cir. 2004). Universities profit by owning and having the right to license patents from their federally-funded research. The government retains the right to march-in and grant licenses to the invention for lack of "effective steps to achieve practical application of the subject invention," i.e., commercialization. 35 U.S.C. § 203 (a)(i).

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4. *See, e.g.*, 35 U.S.C. § 271(d)(4) (refusal to license not misuse); *SCM Corp. v. Xerox Corp.*, 645 F.2d 1195 (2d Cir. 1981) (unilateral refusal to license not antitrust violation).

Furthermore, patent licensing is critical to settlement of patent disputes. One of the most common ways to settle a dispute over patent rights, either before or during litigation, is through a license. Indeed, ppromotion of settlement of litigation in general, and patent litigation in particular, constitutes strong federal policy.[5]

> Public policy strongly favors settlement of disputes without litigation. Settlement is of particular value in patent litigation, the nature of which is often inordinately complex and time consuming. Settlement agreements should therefore be upheld whenever equitable and policy considerations so permit. By such agreements are the burdens of trial spared to the parties, to other litigants waiting their turn before over-burdened courts, and to the citizens whose taxes support the latter.

*Aro Corp. v. Allied Witan Co.*, 531 F.2d 1368, 1372 (6th Cir. 1975) (Markey, C.J., sitting by designation). Both the Federal

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5. *See, e.g., Callen v. Penn.R.R. Co.*, 332 U.S. 625, 630 (1948); *Asberry v. U. S. Postal Serv.*, 692 F.2d 1378 (Fed. Cir. 1982); *Hemstreet v. Spiegel, Inc.*, 851 F.2d 348, 350 (Fed. Cir. 1988); *Flex-Foot, Inc. v. CRP, Inc.*, 238 F.3d 1362, 1369-70 (Fed. Cir. 2001). *See also Schering-Plough Corp. v. FTC*, 402 F.3d 1056, 1075 (11th Cir. 2005), *cert. denied*, 74 U.S.L.W. 3722 (Jun. 26, 2006) ("[t]here is no question that settlements provide a number of private and social benefits as opposed to the inveterate and costly effects of litigation."); *Asahi Glass Co. v. Pentech Pharms., Inc.*, 289 F. Supp. 2d 986, 991 (N.D. Ill. 2003) (Posner, J., sitting by designation) ("[t]he general policy of the law is to favor the settlement of litigation, and the policy extends to the settlement of patent infringement suits.").

Rules of Civil Procedure and the Federal Rules of Evidence have been tailored specifically to promote settlement. *See Advanced Cardiovascular Inc. v. Medtronic, Inc.*, 265 F.3d 1294, 1308 (Fed. Cir. 2001) (FED. R. EVID. 408); *Marek v. Chesny*, 473 U.S. 1, 5 (1985) (FED. R. CIV. P. 68).[6]

Settlement of a patent infringement suit with a license is a rational and mutually advantageous arrangement that removes the parties' uncertainty about the scope or validity of a patent. An accused infringer may practice the invention without fear of infringement liability in exchange for some consideration to the patentee. Both parties benefit and the courts are spared from having to resolve the dispute.

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6. In *Marek v. Chesny*, 473 U.S. at 5, this Court explained:

> The plain purpose of Rule 68 is to encourage settlement and avoid litigation. The Rule prompts both parties to a suit to evaluate the risks and costs of litigation, and to balance them against the likelihood of success upon trial on the merits.

(*citing Advisory Committee Note on Rules of Civil Procedure, Report of Proposed Amendments*, 5 F.R.D. 433, 483 n. 1 (1946), 28 U.S.C.App., p. 637). This Court went on to note that "[r]ule 68's policy of encouraging settlements is neutral, favoring neither plaintiffs nor defendants; it expresses a clear policy of favoring settlement of *all* lawsuits." *Id.* at 10 (emphasis added). *See also Evans v. Jeff D.*, 475 U.S. 717, 733 (1986) ("[i]n approving the package offer in *Marek v. Chesny* we recognized that a rule prohibiting the comprehensive negotiation of all outstanding issues in a pending case might well preclude the settlement of a substantial number of cases: . . .").

But licensing is attractive only if the parties have the proper incentives. At a minimum, licensing must be more attractive than litigation. Few parties would enter into a settlement that put them is a worse position — i.e., that still allowed the other party to the settlement to sue them with impunity. Allowing a licensee in good standing to attack a licensed patent through a declaratory judgment action would do just that — once an accused infringer is licensed, a patentee is barred from suing the licensee, so long as the licensee complies with its license obligations. *See*, *supra*, Part I.

Under current law, the licensee generally has to materially breach the license in order to establish declaratory judgment jurisdiction, thereby subjecting the licensee to both contract and patent remedies in favor of the patentee. That is, the parties return to basically the *status quo ante* the license. A patentee knows today that, if the licensee later challenges the patent, the patentee will be in no worse a position than had there been no license.

The rule sought by the Petitioner would have the effect of giving a licensee an unfettered right to challenge the patent, at the time of its choosing, without fear of infringement liability or an injunction, for only the cost of its royalties and litigation expense. A licensee would have everything to gain and, at worst, would end up back in the position it was in before the litigation.

This would be profoundly unfair. As the Federal Circuit reasoned in *Gen-Probe Inc. v. Vysis Inc.*,

> Vysis voluntarily relinquished its statutory right to exclude by granting Gen-Probe a nonexclusive

> license. In so doing, Vysis chose to avoid litigation as an avenue of enforcing its rights. Allowing this action to proceed would effectively defeat those contractual covenants and discourage patentees from granting licenses. In other words, in this situation, the licensor would bear all the risk, while licensee would benefit from the license's effective cap on damages or royalties in the event its challenge to the patent's scope or validity fails.

*Gen-Probe Inc. v. Vysis, Inc.*, 359 F.3d 1376, 1382 (Fed. Cir. 2004).

A moral dilemma also could arise from the fact that a potential licensee would have a strong incentive to enter into a license while still contemplating initiation of a declaratory judgment action thereafter. Under Petitioner's proposed rule, a patentee would be powerless to stop an accused infringer from taking a license in bad faith and then proceeding directly from the bargaining table to the courthouse.

Under such a proposed rule, patentees would be less likely to grant licenses rather than litigate. Indeed, patentees could be expected to sue and aggressively litigate rather than settle potential litigation — if only to have the eventual settlement incorporated into a consent judgment to which claim and issue preclusion would apply.

## CONCLUSION

For the foregoing reasons, the judgment of Federal Circuit dismissing Petitioner's declaratory judgment action should be affirmed because the inability of Respondents to sue Petitioner mandates that Petitioner likewise be barred from suing Respondents.

Respectfully submitted,

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IN THE
# Supreme Court of the United States

MEDIMMUNE, INC., PETITIONER,

v.

GENENTECH, INC., ET AL., RESPONDENTS.

*ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT*

## AMICUS BRIEF FOR PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA SUPPORTING RESPONDENTS

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## INTEREST OF AMICUS [1]

The Pharmaceutical Research and Manufacturers of America ("PhRMA") is a voluntary, nonprofit association representing the nation's leading research-based pharmaceutical and biotechnology companies. Member companies are in the business of developing new drugs – a complex process involving huge expenditures of time and money. Collectively, PhRMA members are responsible for a huge portion of the innovative medicines approved for use in the United States in the past several decades. In 2005, PhRMA members invested an estimated $39.4 billion toward the discovery and development of new medicines.

Pharmaceutical companies spend many years working to develop each new drug that appears on the market, as well as many that will never earn approval. The process typically begins with creating a new compound or screening hundreds of thousands of existing compounds. The most promising compounds are then modified to optimize their properties, thus producing a candidate drug. Selected compounds are then tested in the lab and in animals to determine whether they might effectively and safely treat a disease. This is followed by clinical trials in normal human volunteers and a series of studies in a relatively small number of patients. The next stage of development is a series of large clinical trials testing the effectiveness as well as the safety of a drug in patients. These clinical trials, typically taking six to eight years, precede the process of seeking approval from the Food and Drug Administration ("FDA"). Altogether, the entire drug development process might last upwards of fifteen years.

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[1] The parties have consented to the filing of this brief. No party authored the brief in whole or in part or contributed monetarily to its preparation or submission. A list of PhRMA's members may be found at http://www.phrma.org/member_company_list.

Practicing in an industry where research and development are expensive and competition is fierce, PhRMA's members depend on strong patent protection to help recoup the investments necessary to develop new medicines. The "reasonable apprehension" test applied by the Federal Circuit in this case provides important patent protection for PhRMA's members. PhRMA files this brief to caution against disavowing the "reasonable apprehension" test in this case.

## ARGUMENT

### I. THE COURT NEED NOT DECIDE WHETHER ARTICLE III MANDATES THE "REASONABLE APPREHENSION" TEST IN ALL SETTINGS.

The Court of Appeals for the Federal Circuit upheld the dismissal of this action on the ground that Petitioner, as a licensee in good standing, had no "reasonable apprehension" of being sued for patent infringement by Respondents. In the court's view, a potential infringer must have a "reasonable apprehension" of being sued for infringement to present a case or controversy sufficiently real and immediate to support the exercise of Article III jurisdiction. Pet. App. 4a-9a.

Petitioner and its *amici* urge the Court to disapprove the Federal Circuit's "reasonable apprehension" test categorically as more restrictive than Article III requires and therefore not a proper basis for dismissal. Pet. Br. 22-28; US Br. 14-19; GPhA Br. 10-13. But the test cannot be considered apart from the setting in which it is applied, and the Court should not here prejudge the test's application in other settings. *Cf. Johnson* v. *United States*, 333 U.S. 46, 56 (1948) (Frankfurter, J., joined by Jackson & Burton, JJ., dissenting in part) ("One cannot be unmindful that 'the radiating potencies of a decision may go beyond the actual holding.'") (citation omitted).

The Court granted review here not to decide whether Article III mandates the "reasonable apprehension" test, but to decide whether Article III "require[s] a patent licensee to refuse to pay royalties and commit material breach of the license agreement before suing to declare the patent invalid, unenforceable or not infringed." That question goes to the rights and duties of licensees and licensors, a field shaped by three centuries of common law. Resp. Br. 29-30. GPhA, as *amicus*, urges the Court to review the application of the "reasonable apprehension" test in the Hatch-Waxman setting. *See* GPhA Br. 2, 4, 8-9. But the application of the test in that setting implicates issues different from those implicated here. Whether to consider the test's application in that setting is the subject of a pending petition for review in *Apotex, Inc.* v. *Pfizer Inc.*, No. 05-1006. The Court should not rule in this case on the validity of the test in that setting.

Although the answer to the question on which the Court granted review has potentially broad implications, the question itself is narrow, and the answer should be no broader than the question. *See, e.g., Greater New Orleans Broad. Ass'n, Inc.* v. *United States*, 527 U.S. 173, 184 (1999). As discussed by Respondents and their *amici*, the Federal Circuit's judgment can be affirmed without resort to the "reasonable apprehension" test. *Cf. Chevron U.S.A., Inc.* v. *NRDC, Inc.*, 467 U.S. 837, 842 (1984) ("[T]his Court reviews judgments, not opinions."). The Court could even affirm the judgment below without reaching the Article III issue. *See* Resp. Br. 35-45; ABA Br. 17-19. Because the "reasonable apprehension" test may have utility in other contexts, the Court should avoid a decision here that might bear on the application of the test in other contexts.

## II. ALTERNATIVELY, ARTICLE III REQUIRES THE "REASONABLE APPREHENSION" TEST.

Article III limits the jurisdiction of federal courts to actual "cases" or "controversies." For an actual case or con-

troversy to exist, Article III requires a "substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *Md. Cas. Co.* v. *Pac. Coal & Oil Co.*, 312 U.S. 270, 273 (1941). Congress cannot expand the jurisdiction of the federal courts beyond the limits set by Article III and therefore cannot confer jurisdiction where an actual case or controversy does not exist. *See, e.g., Verlinden B.V.* v. *Cent. Bank of Nig.*, 461 U.S. 480, 491 (1983).

Accordingly, from the earliest days of the Declaratory Judgment Act, the Court has recognized that a declaratory judgment action may be brought only in "a concrete case admitting of an immediate and definitive determination of the legal rights of the parties in an adversary proceeding." *Aetna Life Ins. Co.* v. *Haworth*, 300 U.S. 227, 241 (1937). Lower courts have long employed the "reasonable apprehension" test in patent cases to implement Article III's requirements of concreteness and immediacy. *See, e.g., Japan Gas Lighter Ass'n* v. *Ronson Corp.*, 257 F. Supp. 219, 237 (D.N.J. 1966). The test has been applied in trademark and copyright cases as well. *See, e.g., Starter Corp.* v. *Converse, Inc.*, 84 F.3d 592 (2d Cir. 1996) (trademark); *United Christian Scientists* v. *Christian Sci. Bd. of Dirs.*, 829 F.2d 1152 (D.C. Cir. 1987) (copyright). The "reasonable apprehension" test is not simply a prudential rule but an aspect of Article III. *See, e.g., Fina Oil & Chem. Co.* v. *Ewen*, 123 F.3d 1466, 1471 (Fed. Cir. 1997) (stating that the reasonable apprehension test "respects the constitutional requirement of an actual controversy"); *Interdynamics, Inc.* v. *Firma Wolf*, 698 F.2d 157, 166 (3d Cir. 1982) (citation omitted) (stating that the reasonable apprehension standard is "identical to the constitutional requirement of 'cases' and 'controversies'").

A patent license permits the licensee to practice a patented invention in return for making royalty payments to the licensor. As long as the licensee pays the royalties and

otherwise satisfies the terms of the license, the licensee may practice the invention, and the licensor may not sue the licensee for infringement. *See, e.g., Ortho Pharm. Corp.* v. *Genetics Inst., Inc.*, 52 F.3d 1026, 1031 (Fed. Cir. 1995). By definition, such a licensee cannot have a "reasonable apprehension" of an infringement suit by the licensor. Any claim by such a licensee that the patent is invalid is necessarily "conjectural or hypothetical," *Steel Co.* v. *Citizens for a Better Env't*, 523 U.S. 83, 103 (1998), and therefore does not satisfy Article III's case-or-controversy requirement. (To be sure, if the licensor sues the licensee for infringement, the licensee may seek a declaration that the patent is invalid. *See Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 508 U.S. 83 (1993). That, however, is because the suit brought by the licensor makes the issue of validity immediate and real.)

GPhA suggests that the "reasonable apprehension" test would bar an infringer from seeking a declaration of invalidity where the patentee has elected to sue infringers separately and has not yet sued the infringer. GPhA Br. 13. Whether such an infringer has a "reasonable apprehension" of suit sufficient to vest a federal court with subject matter jurisdiction will depend on the particular facts of the case. *See, e.g., Gen-Probe Inc.* v. *Vysis, Inc.*, 359 F.3d 1376, 1380 (Fed. Cir. 2004) (noting that the existence of subject matter jurisdiction under the "reasonable apprehension" test depends on the "totality of the circumstances"). Standing alone, however, a patentee's failure to sue a putative infringer cannot give rise to a "case or controversy," even if that patentee has sued other infringers.

GPhA is likewise mistaken in its criticism of the Federal Circuit's rule in *Teva Pharmaceuticals USA, Inc.* v. *Pfizer Inc.*, 395 F.3d 1324 (Fed. Cir. 2005). In that case, a patentee declined to exercise its statutory right to sue a potential infringer for infringement because the patentee did "not wish to expose the patent to the possibility of a noninfringement or invalidity determination." *Id.* at 1334.

The Federal Circuit affirmed the lower court's dismissal of the potential infringer's declaratory judgment action as lacking the immediacy required by Article III.

This case obviously does not present the same issues. In *Teva*, the patentee could have sued the alleged infringer. Here, Respondents cannot sue Petitioner because they have granted Petitioner the right to practice the patented invention in return for royalty payments. As long as Petitioner makes those payments and otherwise complies with the license's terms, it faces no threat of an enforcement action, imminent or otherwise, and there is no case or controversy of sufficient concreteness and immediacy to justify the intervention of the federal courts.

In any event, the Court has long recognized that, in order to bring a declaratory judgment action, a party must face a real prospect of suffering adverse consequences in the absence of a binding judicial determination on a disputed matter. This rule applies even where a party contemplates action that might violate a criminal statute: To seek prospective relief, a party must show a "genuine threat of enforcement." *See Steffel* v. *Thompson*, 415 U.S. 452, 475 (1974). Thus, for example, in *Boyle* v. *Landry*, 401 U.S. 77, 81 (1971), the Court refused to issue a declaratory judgment because there was no "specific threat by any officer or official . . . to arrest or prosecute" the plaintiffs; resolution of the issue therefore would have constituted impermissible "speculation about the future." *See also* 10B Charles Alan Wright, *et al.*, *Federal Practice and Procedure* § 2757, at 477-84 (3d ed. 1998) ("[C]ourts have declined to hear cases seeking a declaratory judgment on the constitutionality of a particular statute or ordinance when plaintiff has not shown that there is any immediate threat that the statute will be enforced against him."). Like parties who may not challenge state laws in the absence of a threat of enforcement, patent infringers are precluded from seeking declaratory judgments where the patentees have disavowed any intention to sue.

In light of these principles, the Federal Circuit's "concern for protecting 'quiescent' patentees," GPhA Br. 16, is legitimate. Contrary to GPhA's suggestion, *id.* at 17, the Federal Circuit in *Hunter Douglas, Inc.* v. *Harmonic Design, Inc.*, 153 F.3d 1318 (Fed. Cir. 1998), decided that it lacked jurisdiction not because the "reasonable apprehension" test protects quiescent patent holders, but because to have decided the question in that case would have been to "render[ ] a forbidden advisory opinion," *id.* at 1326 (citation and internal quotations omitted). Given the Court's repeated admonitions that a party must face a genuine threat of enforcement before seeking a declaratory judgment, it is hardly surprising that potential infringers of a quiescent patentee may not hale the patentee into court *willy-nilly*.

Federal courts have long required more than a hypothetical possibility of an infringement suit to ground declaratory judgment jurisdiction. As the Court has stated:

> The difference between an abstract question and a "controversy' contemplated by the Declaratory Judgment Act is necessarily one of degree . . . Basically, the question in each case is whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.

*Md. Cas. Co.*, 312 U.S. at 273.[2] As stated by one District Court:

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[2] *See also EMC Corp.* v. *Norand Corp.*, 89 F.3d 807, 811 (Fed. Cir. 1996) ("This court's two-part test for declaratory judgment jurisdiction is designed to police the sometimes subtle line between cases in which the parties have adverse interests and cases in which those adverse inter-

(continued...)

> In the absence of strong objective evidence sufficient to indicate intent to initiate an enforcement action, the mere listing of multiple patents does not create declaratory judgment jurisdiction . . . [where the generic manufacturer] has not alleged objective words or actions by [the innovator] that demonstrate an intent to enforce its patent rights . . . either through explicit threats or indirect threats or actions that place the declaratory plaintiff in reasonable apprehension of suit.

*Dr. Reddy's Labs., Ltd.* v. *Pfizer Inc.*, No. 03-CV-726, 2003 WL 21638254, at *5-6 (D.N.J. July 8, 2003). Instructing federal courts to assume jurisdiction over cases in which a patentee has taken no specific actions against an infringer or potential infringer would violate these long-standing principles, and would have the effect of courts issuing advisory opinions in violation of Article III's jurisdictional limitations.

For these reasons, there is no basis in law for asserting that the reasonable apprehension test is *not* constitutionally required or that the test, when applied appropriately, is not aligned with the requirements of Article III. Instead, the correct understanding of the law is that courts are required to assess, on a case-by-case basis, whether there are specific facts in the record to satisfy the consti-

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ests have ripened into a dispute that may properly be deemed a controversy."); *Phillips Plastics Corp.* v. *Kato Hatsujou Kabushiki Kaisha*, 57 F.3d 1051, 1053 (Fed. Cir. 1995) (citations omitted) ("[T]o create an actual controversy . . . [t]here must be action by the patent holder sufficient to create an objectively reasonable apprehension that suit will be brought against the declaratory plaintiff."); *BP Chems. Ltd.* v. *Union Carbide Corp.*, 4 F.3d 975, 978 (Fed. Cir. 1993) ("[M]ore is required than the existence of an adversely held patent.").

tutional requirement of an actual case or controversy, including whether there is a reasonable apprehension of suit.

Finally, GPhA urges that the "equalizing principles" that the Federal Circuit reasoned underlie the Declaratory Judgment Act are not recognized by this Court. GPhA Br. 18-20. But the policies relied on by the Federal Circuit in implementing the Declaratory Judgment Act's requirements here are entirely consistent with both the Declaratory Judgment Act and this Court's cases.

As the Federal Circuit has explained, the purpose of the Declaratory Judgment Act is to

> enable a person who is reasonably at legal risk because of an unresolved dispute, to obtain judicial resolution of that dispute without having to await the commencement of legal action by the other side. It accommodates the practical situation wherein the interests of one side to the dispute may be served by delay in taking legal action.

*BP Chems. Ltd.* v. *Union Carbide Corp.*, 4 F.3d 975, 977 (Fed. Cir. 1993).

In this case, Respondents hold no procedural advantage over Petitioner. On the contrary, Respondents are barred from bringing an infringement action against Petitioner by the license agreement. Thus, under the Federal Circuit's rule, *neither* party may presently bring an action against the other. Under the rule urged by Petitioner, it would have a right to institute an action against Respondents, while Respondents could not sue it for infringement. The Declaratory Judgment Act was designed to prevent just such inequality.

*Maryland Casualty*, 312 U.S. 270, is not to the contrary. In that case, an insurer sought a declaratory judgment against its insured and a third party stating that its policy did not cover the third party's claim against the in-

sured. It was beyond dispute that the insurer's claim against the insured was of sufficient immediacy to present an actual controversy under Article III; the insurer's suit against the insured was the mirror-image of the affirmative suit that the insured could have brought against it.

The Court also concluded that the insurer's claim against the third party could proceed, even though the third party could not sue the insurer until after the insured failed to satisfy a judgment in the insurer's favor. The Court's conclusion, however, was based on a fact not present in this case – the possibility of inconsistent judgments in the federal-court proceeding between the insurer and the insured and a later state-court proceeding between the insured and the third party. *See id.* at 274. Thus, *Maryland Casualty* does not undermine the principles of equality and fairness that underlie the Declaratory Judgment Act and antithetical to the role proposed by Petitioner in this case.

## III. CONGRESS AFFIRMED THE "REASONABLE APPREHENSION" TEST WHEN IT AMENDED HATCH-WAXMAN IN 2003.

Petitioner and its *amici* assert that Congress enacted the Declaratory Judgment Act, in part, to enable a party to seek a judicial determination of non-infringement or invalidity before undertaking activity that could subject the party to potentially ruinous liability. *See* Pet. Br. 29-33; U.S. Br. 9, 19; GPhA Br. 5-7. This general proposition, to the extent that it is accurate, is irrelevant here. Whatever prospective declaratory relief Congress meant to make available to a party wishing to engage in potentially infringing conduct, Congress did not mean to make avail-

able to parties who had purchased immunity from infringement actions.[3]

GPhA asserts that 2003 amendments to the Hatch-Waxman Act "confirmed" the Declaratory Judgment Act's policy in favor of allowing a party wishing to engage in potentially infringing activity to seek a prospective declaration of non-infringement or invalidity. GPhA Br. 7-9. In fact, notwithstanding GPhA's incantation of Congress' desire to foster "patent certainty," *id.* at 8, Congress affirmed its intent to preserve the "reasonable apprehension" test as developed by the courts, and to preclude Declaratory Judgment Actions by potential infringers based on the simple fact that the patentee had not sued.

In the 2003 amendments, Congress provided that when an ANDA includes a paragraph IV certification, and neither the NDA holder nor the patent owner has brought an action for infringement of the patent before the expiration of 45 days after notice of the paragraph IV certification was received, the federal courts have subject matter jurisdiction in a suit brought under the Declaratory Judg-

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[3] "Congress is understood to legislate against a background of common-law . . . principles." *Astoria Fed. Sav. & Loan Ass'n v. Solimino*, 501 U.S. 104, 108 (1991). When Congress enacted the Declaratory Judgment Act in 1934, the common-law principle of licensee estoppel barred a nonbreaching licensee from challenging the patent. To have authorized a suit such as this would have meant abrogating that principle. *See* ABA Br. 6-10. But "[i]n order to abrogate a common-law principle, [a] statute must 'speak directly' to the question addressed by the common law." *United States* v. *Texas*, 507 U.S. 529, 534 (1993) (citation omitted). In enacting the Declaratory Judgment Act, Congress did not "speak directly" to that issue.

ment Act to the extent consistent with the Constitution.[4] The Conference Report sets out Congress's intent with respect to "reasonable apprehension":

> DECLARATORY JUDGMENTS
>
> The conferees expect that courts will find jurisdiction, where appropriate, to prevent an improper effort to delay infringement litigation between generic drug manufacturers and pioneer drug companies. The conferees expect courts to apply the "reasonable apprehension" test in a manner that provides generic drug manufacturers appropriate access to declaratory judgment relief to the extent required by Article III.
>
> Through the modifications in this Act, the conferees do not intend for the courts to modify their application of the requirements under Article III that a declaratory judgment plaintiff must, to the extent required by the Constitution, demonstrate a "reasonable apprehension" of suit to establish jurisdiction. *See, e.g., Fina Oil & Chem. Co.* v. *Ewen*, 123 F.3d 1466, 1471 (Fed. Cir. 1997). The conferees expect the courts to examine as part of their analysis the particular policies served by the Hatch-Waxman Act.
>
> In determining whether a reasonable apprehension of suit exists where an ANDA has been filed with a paragraph IV certification and the patentee has not brought an infringement suit within the 45

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[4] Pub. L. No. 108-173, tit. XI, § 1101(a)(2)(C), 117 Stat. 2066, 2450 (2003) (codified at 21 U.S.C. § 355(j)(5)(C)(i)); § 1101(b)(2)(D), 117 Stat. 2066, 2454 (2003) (codified at 21 U.S.C. § 355(c)(3)(D)); § 1101(d), 117 Stat. 2066, 2457 (codified at 35 U.S.C. § 271(e)(5)).

> days, the conferees expect courts to examine these specific factors as part of the totality of the circumstances. *See, e.g., Vanguard Research, Inc.* v. *Peat, Inc.*, 304 F.3d 1249, 1254 (Fed. Cir. 2002). In any given case, the conferees expect a court may ***or may not*** find a reasonable apprehension of suit where these two specific factors are present.

Conference Report, H.R. Rep. No. 108-391, at 617 (2003), *reprinted in* U.S.C.C.A.N. 1808, 2187 (emphasis added). *See Apotex, Inc.* v. *Pfizer Inc.*, 385 F. Supp. 2d 187, 193 (S.D.N.Y. 2005) (discussing legislative history of 2003 amendment), *aff'd*, 199 Fed. Appx. 1013 (Fed. Cir. 2005) (per curiam), *petition for cert. pending*, No. 05-1006.[5]

Of course, the policy reflected in these amendments – to allow an ANDA applicant to pursue a declaratory judgment action where it has a "reasonable apprehension" of suit – resonates in this case. The mere fact that an infringer faces potentially significant liability by virtue of the patentee's ability to enforce its patent does not give rise to a case or controversy. Taking into account the totality of the circumstances, there must be conduct that gives rise to a "reasonable apprehension" suit, and that is absent where, as here, the party seeking declaratory relief has purchased immunity from an infringement action. Such a party is legally entitled to practice the patented invention under the license agreement and therefore has no need of declaratory relief.

## CONCLUSION

For the foregoing reasons, the judgment should be affirmed.

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[5] On May 15, 2006, the Court invited the Solicitor General to file a brief in this case expressing the views of the United States.

Respectfully submitted,

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In The
# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

v.

GENENTECH, INC. AND CITY OF HOPE NATIONAL MEDICAL CENTER,

*Respondents.*

**On Writ Of Certiorari To The United States Court Of Appeals For The Federal Circuit**

## BRIEF OF PROFESSORS JOHN R. ALLISON, DANIEL R. CAHOY, CHRISTOPHER A. COTROPIA, THOMAS F. COTTER, SUZANNE E. ECKES, THOMAS G. FIELD, JR., MICHAEL S. MIRELES, SEAN O'CONNOR, AND KRISTEN R. OSENGA AS *AMICI CURIAE* IN SUPPORT OF THE RESPONDENTS

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## INTEREST OF *AMICI CURIAE*

*Amici* are scholars at American law, business, and education schools who teach, write about, or have an interest in patents and intellectual property law. *Amici* have no stake in the outcome of this case, and we file this brief solely as individuals and not on behalf of the institutions with which we are affiliated.[1] We are, however, interested in assisting this Court to interpret the law in a way that is both consistent with the intent of Congress and that best promotes the development and disclosure of new inventions. A list of *amici* is appended to the signature page. Both petitioner and respondents have consented to the filing of this brief.

## SUMMARY OF ARGUMENT

Current law already permits a patent licensee to challenge patent validity when the license has been breached or terminated, or at any time by requesting that the United States Patent and Trademark Office conduct a patent reexamination. It does not permit the licensee to commence a civil action seeking a declaratory judgment of patent invalidity, however, while the license remains in force. We believe that petitioner MedImmune's proposed rule, one that would permit licensees to commence declaratory judgment proceedings at any time, would undermine sound patent policy and decrease consumer welfare by increasing the cost of patent licensing without a commensurate social benefit. We also have grave doubts

[1] Pursuant to Rule 37.6, no party other than the signatories has authored or paid for any part of this brief, except that Farella, Braun + Martel LLP has paid the copying, binding and service costs for this brief.

concerning the existence of a case or controversy in cases in which the licensee continues to perform under the license, but we leave the argument of that issue to the parties and other *amici* and instead focus on the matter most clearly within our own area of expertise, namely patent policy.

The licensing of patent technology is a crucial aspect of any patent system. Licensees are often better positioned than patent owners to efficiently manufacture or market products that incorporate patented inventions. Licensing therefore generally reduces price and increases output, delivering the invention to more consumers at a lower price. Parties to licensing agreements nevertheless often bargain under circumstances of substantial risk, uncertainty, and transaction costs, all of which to some extent reduce the potential gains from trade. Rules that would further increase the cost and uncertainty of patent licensing, such as the rule sought here by petitioner MedImmune, threaten to further impede the efficient exploitation of patented technology, thus potentially making the parties and, more importantly, consumers, worse off.

We further argue that petitioner's proposed rule would generate few if any corresponding social benefits, in terms of increasing the opportunities for challenging invalid patents, to justify the aforementioned social costs. As the law now stands, licensees and others have several options available for challenging patent validity under appropriate circumstances; and Congress may if it chooses enact yet other measures. Modifying the existing case law in the manner proposed by petitioner, however, is required neither by this Court's decision in *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969), nor by considerations of sound patent policy.

## ARGUMENT

### I. Sound Patent Policy Counsels Against a Rule Permitting Licensees to Institute Validity Challenges While Continuing to Perform Under Their Licenses.

We begin our analysis by conceding an obvious point: that the United States Patent Office grants a large number of patents that fail to satisfy one or more of the conditions necessary for patent validity. This observation is borne out by the substantial plurality of litigated patents that are ultimately invalidated. *See* John R. Allison & Mark A. Lemley, *Empirical Evidence on the Validity of Litigated Patents*, 26 AIPLA Q.J. 185, 205-07 (1998); Kimberly A. Moore, *Judges, Juries, and Patent Cases – An Empirical Look Inside the Black Box*, 99 Mich. L. Rev. 365, 391 (2000). Patentee efforts to exercise rights under invalid patents can impose a variety of social costs, including unnecessary administrative and transaction costs and, in the case of patents that confer a degree of market power, deadweight loss. These costs can have the perverse effect of retarding rather than stimulating innovation, in contravention of the constitutional purpose of "promot[ing] the Progress of . . . the Useful Arts." U.S. Const., art. I, sec. 8, cl. 8. Nevertheless, we conclude that the rule proposed by petitioner MedImmune – one that would permit patent licensees to institute challenges to patent validity while continuing to enjoy the benefits of their licenses – would be a counterproductive response to the flaws of the current patent regime. By contrast, the rule currently followed by the United States Court of Appeals for the Federal Circuit, which allows licensee challenges only after the license has been breached or terminated, recognizes the procompetitive and proconsumer benefits of enabling the licensing

parties to shift some of the risk of a subsequent determination of patent invalidity from patentee to licensee; the Federal Circuit's rule is, moreover, fully consistent with this Court's decision in *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969). We therefore urge this Court to enter a judgment of affirmance.

### A. Efficient Licensing is Essential to the Proper Functioning of the Patent System.

As this Court has recognized on many occasions, a fundamental premise of the patent system is that the granting of exclusive rights in inventions and discoveries for a limited time stimulates both the creation of new technology and its disclosure to the general public. *See, e.g., Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480 (1974). Absent a patent system or some other market correcting mechanism, inventors would be less willing to invest either in the production or disclosure of new inventions, due to the threat posed by free riders. At the same time, a variety of patent doctrines reflect the need to balance the social benefits provided by exclusive rights against the social costs, including transaction and monopoly costs, to which an overly expansive regime of patent rights would give rise. Ideally, the patent system strives to achieve the maximum surplus of benefits over costs and thus to fulfill the constitutional mandate of promoting the progress of the useful arts. In large part, and despite many imperfections, the U.S. patent system has distinguished itself in its efforts to attain this goal.

An important subset of patent doctrine relates to the licensing of patented inventions. Many patentees lack the capability of efficiently exploiting their patented inventions

by means of their own manufacture, use, or sale of the patented technology. For example, a patent owner may be able to manufacture or market products embodying its invention only at higher cost, or on a smaller scale, than could a firm that specializes in the manufacture or sale of a specific type of product. The ability to license patented inventions therefore promises a higher return on investment to the patentee, who is thereby better able to exploit the value of the invention, and renders better off those firms that can specialize in the manufacture, sale, or use of the relevant technology. *See, e.g.*, Roger D. Blair & Thomas F. Cotter, *The Elusive Logic of Standing Doctrine in Intellectual Property Law*, 74 Tulane L. Rev. 1323, 1333-34 (2000). More importantly, patent licensing in general makes consumers better off, by lowering the cost (and thus the price) of manufacturing and marketing products embodying patented inventions, by expanding output, and – as a matter of economic logic, since a reduction in price and expansion of output necessarily increases consumer surplus beyond what it otherwise would be – by reducing deadweight loss. It follows that, in general, legal rules that promote and enable technology licensing are a social good, at least in the absence of antitrust problems or other countervailing considerations that on occasion may arise. This point has not been lost on legal policymakers. Over the past twenty to thirty years, for example, federal antitrust enforcers have come to recognize the procon-sumer benefits of licensing and thus are much less apt to challenge licensing arrangements in the absence of compelling proof of anticompetitive harm. *See generally* U.S. Dep't of Justice & Federal Trade Comm'n, Antitrust Guidelines for the Licensing of Intellectual Property (Apr. 6, 1995).

Even so, licensing remains an undertaking that is fraught with peril. On the one hand, when a technology is new, no one may yet have a clear idea how it is best utilized, whether consumers will respond favorably to it, or whether other competing technologies will prove superior; in short, no one may appreciate just how valuable (or valueless) the technology is likely to be. On the other hand, even when a technology is more mature, no one may be able to predict whether it will yet be put to hitherto undiscovered uses – or, alternatively, how quickly it will obsolesce. This uncertainty can reduce the gains from trade that might otherwise be available to the licensing parties. *See, e.g.*, Richard E. Caves et al., *The Imperfect Market for Technology Licenses*, 45 Oxford Bull. Econ. & Stat. 249 (1983) (discussing various market imperfections in the licensing of technology); Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 Tex. L. Rev. 989, 1053-54 (1997) (discussing high transaction costs associated with licensing). Legal rules that make it more difficult to license patented inventions therefore are likely, on average, to decrease rather than increase consumer welfare, absent clear proof of anticompetitive or other countervailing harm.

### B. Allowing Patent Licensees to Institute Validity Challenges While Still Enjoying the Benefits of Their Licenses Would Likely Raise the Cost of Patent Licensing, and Thus Decrease Consumer Welfare.

As the law now stands, a party considering the manufacture, use, or sale of technology that is covered by another's existing patent has several options. First, it may decide to make, use, or sell despite the existence of the

patent, and if sued or threatened with suit to defend on the ground of invalidity or noninfringement. Second, it may decide to "design around" the patent so as to achieve the same end result without use of the claimed invention. Third, it may decide to license the invention from the patent owner on terms that take into account both the value that the licensee expects to extract from the invention and the probability that the patent is both valid and "reads on" the licensee's proposed conduct. To illustrate by means of a simple example, assume that a potential licensee's use of the patented invention is expected to bring in $1,000 of profit, over a given time period, above that which could be gained from the use of the next-best alternative; thus if the would-be licensee were to use the invention without permission, its expected profit would consist of this $1,000 minus the expected costs of litigation. These costs would include, among other things, an estimate of the user's potential damages liability, based upon its assessment of the probability of patent validity and infringement, and attorney's fees. If the would-be user estimates (1) the probability of patent validity and infringement to be 50%; (2) its damages in the event it is found to have infringed to be $600; and (3) its attorneys' fees to be $100, its expected gain from unauthorized use equals $600. A risk-neutral user therefore would agree to pay no more than $400 ($1,000 minus $600) for permission to use the invention. Presumably the patent owner will make its own cost-benefit calculation in determining how much it is willing to accept in exchange for granting a license; if this amount is no more than $400, the parties will find it in their mutual interest to agree to a license, absent prohibitive transaction costs or other bargaining obstacles.

Not surprisingly, the real world often presents many additional complications. For one thing, patent litigation is notoriously expensive. *See, e.g.*, American Intellectual Property Law Association, 2005 Report of the Economic Survey 22-23 (reporting estimated mean and median costs for small, middle, and high stakes patent litigation, with high stakes litigation resulting in estimated mean total costs of more than $5 million and median total costs in excess of $4 million). It is, therefore, often in both parties' interest to avoid litigation by agreeing to a license – which thus can be thought of as a prelitigation settlement of a hypothetical future patent dispute. (Of course, licenses often arise later on as well, as part of an actual settlement of an actual dispute). In addition, both the inherent value of the invention and the probability of validity and infringement may be uncertain; either or both parties may be risk-averse, meaning that they would turn down an actuarially fair "bet" on future events unless offered a sufficient risk premium; and each party's evaluation of its own and the other party's likely costs and benefits may differ due to asymmetric information. Financial constraints also may limit either or both parties' options in various ways. A licensee, for example, may prefer a smaller initial royalty coupled with future payments based on use, due to liquidity constraints; the licensor, on the other hand, may prefer a larger down payment and a fixed rather than per-use royalty that does not discourage the licensee from optimal future use. The existence of so many uncertain variables can lead to a wide variety of rational licensing arrangements, including exclusive and nonexclusive licenses, lump-sum and running royalty rates, and other permutations. *See* Blair & Cotter, *supra*, at 1380-1402.

Suppose, then, that a patentee and potential licensee are considering the licensing of an invention; that both parties have the good-faith belief that the patent is valid and would be infringed by the licensee's proposed use; but that, as is virtually always the case, the probability that a future decisionmaker would find both validity and infringement is less than 100%. As noted above, both parties can be expected to take their subjective estimates of validity and noninfringement into account in setting the "price" at which they would be willing to proceed. Now consider the likely consequences of a rule (from which the parties may not deviate by contract) permitting the licensee to challenge patent validity while enjoying the benefits of the patent license, versus a rule that does not permit the licensee to do so (but that does allow the licensee to challenge validity in the event the patentee sues for infringement or breach of contract). The former rule – that is, the rule espoused by petitioner here – requires the patentee to bear the incremental risk that the licensee will mount a successful challenge during the pendency of the license. The latter rule (the rule adopted by the Federal Circuit) would instead shift some of the risk of invalidity to the licensee – though not all of that risk, since a licensee who subsequently becomes convinced that the patent is in fact invalid could stop paying royalties and then assert invalidity if the patentee sues or threatens to sue. The former rule thus creates an incentive for the patentee to demand either more royalties upfront, or higher royalties overall, as compensation for this additional risk. Put another way, the patentee has an incentive to charge each licensee a higher price than would otherwise be the case, insofar as the use of the patent comes coupled with an inalienable option to challenge validity at any time. Licensees who do not expect to mount a validity challenge

and who would prefer to pay a lower rate in exchange for assuming some of the risk of invalidity are therefore rendered worse off, absent some alternative way for them to credibly signal their belief that the patent is valid. At the margin, some licensees may be priced out of the market, or at best will respond to the higher royalty rate by charging more and producing less. Both parties therefore may be worse off than if they had been able to allocate risk in accordance with their own preferences and liquidity constraints.

Another way of thinking about the matter is that petitioner's proposed rule effectively permits one party unilaterally to unravel the pre- or post-litigation settlement of a patent infringement suit that might have arisen, or did arise, absent the license. Unsurprisingly, patent owners may be marginally less willing to enter into such vulnerable settlements in the first instance, or may demand a higher premium in response to the increased uncertainty. A rule that encourages such results runs counter to the general federal policy favoring settlement – a policy that itself is based on many sound considerations, including the high private and public cost of litigation (particularly patent litigation). One might also take note of the potential inequity of allowing one party, but not the other, to do the unraveling of the settlement; the patent owner could not sue the licensee for infringement unless and until the licensee exceeded the scope of the license or the license terminated. On a fairness basis, if not on a purely economic rationale, this asymmetry is troubling.

But it is not only the parties who may be rendered worse off by the inclusion of an unwanted, but mandatory, term permitting licensees to challenge patents pre-breach. The public also may be worse off to the extent the mandatory

term raises the cost to licensees of using patented technology. Economic analysis predicts that the price of goods embodying such technology will increase and that output will decline, thus decreasing consumer surplus. Indeed, consumers may be worse off both short-term, as a result of higher costs and lower output, and in the long run as well, to the extent that the mandatory term marginally decreases the value of patents generally and thus the incentive to invent and disclose. We submit that these potential social costs are not trivial; and that this Court should decline to adopt petitioner's proposed rule absent clear proof of some potentially weightier social benefit.

### C. The Potential Benefits of Petitioner's Proposed Rule Do Not Outweigh the Social Costs.

In response to the preceding argument, we anticipate the argument that the social costs we have identified above, as flowing from the adoption of petitioner's proposed rule, nevertheless could be worth incurring if the social benefits of increased patent invalidation were sufficiently large and could not be achieved in other ways. But the premises of this response seem doubtful, for several reasons.

First, even in the absence of petitioner's proposed rule, potential and former licensees and other would-be users of patented inventions retain other means of challenging possibly invalid patents. As noted, persons who wish to use inventions that are arguably covered by existing patents may do so and then defend themselves, in litigation, on the ground of invalidity – or may institute declaratory judgment actions for invalidity under appropriate circumstances. Any final judgment of patent invalidity is, moreover, binding on

the patent owner vis-à-vis any other possible future disputants. *See Blonder-Tongue Labs., Inc. v. University of Ill. Found.*, 402 U.S. 313, 350 (1971). Alternatively, and consistent with *Lear, Inc. v. Adkins*, licensees themselves may challenge validity when they are sued or threatened with suit for infringement (for example, for continuing to use the patent after license termination) or for breach of contract (*e.g.*, for refusing to pay promised royalties). *See Lear*, 395 U.S. at 660-71. To be sure, the result in *Lear* can be defended on the ground that it would be inequitable to permit a patentee to pursue a claim against its former licensee without permitting the licensee to defend by challenging patent validity. But the balance struck by *Lear* would be upset by MedImmune's rule here. In contrast to the rule in *Lear*, MedImmune's proposed rule would allow the licensee to use a license both as a shield and sword, insulating the licensee from infringement claims while at the same time permitting it to challenge validity, absent any provocation from the patentee.

Second, the Patent Act already permits "[a]ny person at any time" to seek reexamination of an issued patent – that is, to request that the Patent Office reconsider patent validity in light of some overlooked prior art. *See* 35 U.S.C. §§ 301, 302 (2000). As the statute implies, "there are no persons who are excluded from being able to seek reexamination." Manual of Patent Examining Procedure § 2212 (8th ed. 2005); *see also id.* § 2612 (no standing requirement for inter partes reexaminations); 37 C.F.R. §§ 1.510(a), 1.913 (2005) (same); *Vitronics Corp. v. Conceptronic, Inc.*, 36 F. Supp. 2d 440, 441 (D.N.H. 1997). The statute even permits requests for ex parte reexamination to be made anonymously. *See* 35 U.S.C. § 301.

Third, it is clearly within the power of Congress – and to a lesser extent, the courts and the Patent Office itself, in articulating and developing patent policy in accordance with their constitutional powers – to develop yet other effective ways of reducing the number of invalid patents. Patent lawyers and scholars have suggested many possible methods for accomplishing this goal, including greater upfront scrutiny of patent applications for conformity with, among other things, the nonobviousness requirement; extending bounties to persons who come forward with prior art demonstrating that a patent lacks novelty or is obvious; and the adoption of post-grant opposition procedures of the type commonly used within the European Patent Office and in other countries to facilitate early, low-cost resolution of validity disputes. For that matter, Congress could, if it so chose and if such proceedings are permissible under article III of the Constitution, explicitly to allow licensee challenges of the type espoused by petitioner here. The fact remains that Congress has not expressly opted to do so, however; and we submit that Congress's inaction, coupled with the possibility that it may prefer one or more of these other alternatives – or none of them – provides further reason for this Court to stay its hand.

## CONCLUSION

For the reasons stated above, we urge this Court to affirm the judgment of Court of Appeals for the Federal Circuit.

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IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.,

*Petitioner,*

*v.*

GENENTECH, INC., *et al.*,

*Respondents.*

*On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit*

## BRIEF FOR *AMICI CURIAE* QUALCOMM INCORPORATED AND INTERDIGITAL COMMUNICATIONS CORPORATION IN SUPPORT OF RESPONDENTS

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## INTERESTS OF *AMICI CURIAE*[1]

*Amici curiae* QUALCOMM Incorporated and InterDigital Communications Corporation are global leaders in telecommunications technology. They each develop, own, and frequently license patented technology. Between them, they have negotiated thousands of licenses to patented technology, typically based upon the reasonable assumption that a patent licensee cannot at the same time hold them to the terms of a contractual license and challenge the contract's premise. They are concerned that a contrary rule will undermine settled expectations, stifle innovation, and inhibit further licensing.

## SUMMARY OF ARGUMENT

There is little *amici* could add to the thorough defense of the dismissal as a matter of Article III jurisdiction provided by both Genentech and City of Hope. But, as both Genentech and City of Hope make clear, that is not the only ground on which this Court can affirm the judgment. The dismissal can be affirmed also on the alternative ground that MedImmune, as a licensee in good standing, is equitably estopped from challenging the validity of the patent it is licensing.

A business that wishes to use a patented invention without a license faces hard choices and substantial burdens if it believes that the patent is invalid. So, too, does a business that has licensed the invention and is contemplating whether to repudiate the license and challenge the patent. Both face the potential of an injunction and treble damages if

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[1] Pursuant to Supreme Court Rule 37.6, *amici* confirm that no counsel for a party authored this brief in whole or in part and no person or entity other than *amici* or its counsel made a monetary contribution to the preparation or submission of this brief. Letters from the parties consenting to the filing of this brief have been lodged with the Clerk of the Court.

they infringe the patent. Neither has the benefit of a fixed royalty rate guaranteed regardless of the success of their challenge. In contrast, a licensee who sues, but retains the protection of the license, escapes all the burdens and hard choices. Such a licensee enjoys a fixed royalty and immunity from injunctive relief, while still pursuing its challenge to the very premise of the license—that the licensor has a valid patent.

That is not fair, especially to licensors who negotiated licenses in the past based upon the premise—which has been clear law in the Federal Circuit for some time—that the licensee cannot retain the benefits of a license and sue at the same time.

That is why, for hundreds of years, equitable principles have prohibited exactly this sort of duplicity. The rule has long been that a party to a contract in MedImmune's position cannot challenge the validity of any underlying property interest without relinquishing the benefits conveyed. For well over a century, this Court has applied this rule to all sorts of property rights, including intellectual property.

This Court's opinion in *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969), did nothing to alter that fundamental equitable rule. *Lear* involved a licensee who *had* repudiated the license, and had given up all the benefits under the contract. In that case, this Court rejected only the view—which earlier cases had accepted—that once a licensee takes a license, it may *never* sue to challenge the validity of the patent. The principles articulated in *Lear* compel the opposite conclusion when applied to a licensee who challenges the premise of the license but insists on retaining the benefits. Whereas *Lear* was concerned about permanently muzzling parties with the greatest interest in challenging invalid patents, that concern is not implicated here. Under the traditional equitable rule, a licensee is not permanently barred from challenging the validity of the patent; it can always make the decision to forego the benefits of the license in order to sue. To be sure,

there are often consequences to such a decision—a potential injunction and damages, for example. But the Patent Act, itself, imposes those consequences, and it imposes them evenhandedly on infringers who once secured licenses and those who never did.

To allow suits like this one to proceed would be against the public interest. If patent owners cannot be assured of patent peace when licensing their inventions, they will be less inclined to license, and at a minimum will insist on higher royalty rates. Moreover, allowing suits of this sort to proceed will only encourage more litigation, and particularly more meritless litigation, for licensees will have every incentive to sue, on any patent theory, so long as the expected benefits exceed the cost of litigation.

Because the Court of Appeals' decision is infused with equitable considerations, and because there is no question, under preexisting law, that the Court of Appeals would reach the same conclusion on this alternative ground, this Court should reach this argument if it disagrees with the jurisdictional basis of the opinion below. Licensors and licensees, alike, need to know sooner rather than later whether this kind of suit is permissible.

## ARGUMENT

### I. IT IS UNFAIR TO ALLOW A PATENT LICENSEE TO ENJOY THE BENEFITS OF A LICENSE WHILE CHALLENGING THE VERY PREMISE OF THE LICENSE.

Though couched in the drab language of jurisdiction, the principle at stake in this case is a matter of simple fairness. The equitable principle is so well settled, so pervasive, that it comes petrified in proverb. Its provenance dates back nearly five centuries, when it was rendered, "Wolde ye bothe eate your cake, and haue your cake?" John Heywood, *A Dialogue Conteynyng Prouerbes & Epigrammes* 96 (John S. Farmer, ed., Barnes & Noble 1966)

(1562). Writers from Cervantes and Keats to Bob Dylan and Paula Abdul have immortalized it, as it mutated from the once pervasive, "You cannot eat your cake and have it too," John Keats, *On Fame* (1819), *in The Poetical Works of Keats* 142 (Paul D. Sheats, ed., Houghton Mifflin 1975) (1899); Miguel de Cervantes Saavedra, *Don Quixote*, vol. II at 312 (P.A. Motteux trans., Everyman's Library 1991) (1615), to the modern (if oblique), "you can't have your cake and eat it too," Paula Abdul, *One or the Other, on Forever Your Girl* (Virgin Records 1988); Elvis Costello, *Town Where Time Stood Still, on Punch the Clock* (Rykodisc 1995) (1983). *Contra* Bob Dylan, *Lay, Lady, Lay, on Nashville Skyline* (Columbia Records 1969) ("You can have your cake and eat it, too.").

However rendered, the precept is as true as it is trite: You cannot simultaneously take two diametrical positions and exploit the benefits of both stances. It's not fair. From boardrooms, to courtrooms, to school yards, social interactions of all forms demand that we make choices, often difficult choices—and live with their consequences.

That principle lies at the heart of this case. On the one hand, no one questions the freedom of a patent licensee to repudiate the contract and, in derogation of its terms, challenge the validity of the very patent on which the license is premised. This Court guaranteed licensees that freedom in *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969). Conversely, no one questions the right of a licensee to adhere to the contract, and seek the protection of its terms. This case, however, is about whether a licensee can take both positions simultaneously: whether it can act in derogation of the contract while clinging to the contract's benefits. This case is about whether you can have your contract and defeat it, too.

### A. A Licensee Who Sues Without Repudiating the License Avoids All Risks and Burdens Faced By More Scrupulous Businesses.

To appreciate MedImmune's posture, imagine three companies—Nolicense Inc., Renounce Co., and Licensue Co.—all eager to use a patented invention owned by an innovator, say, Genentech. Nolicense Inc. does not secure a license, intending instead to challenge the patent's validity. Renounce Co. secures a license, but repudiates it to challenge the patent. Licensue Co.—like MedImmune—secures a license, but then challenges the patent without repudiating the contract. The first two, whose current stances are internally consistent, face tough choices and serious risks. The latter, alone, takes contradictory positions, and, if permitted to do so, gets a free pass with no burdens, no risks, and no dilemmas.

***The non-licensee's quandary.*** If Nolicense Inc. uses the patented invention without securing a license, Genentech can demand that it cease using the invention. Nolicense Inc. then confronts a quandary: resist or desist. If Nolicense Inc. resists, Genentech can file an infringement action and seek injunctive relief. The district court will likely issue an injunction, unless Nolicense Inc. succeeds in demonstrating that the patent is invalid or unenforceable or the use is non-infringing.[2] *See eBay, Inc. v. MercExchange L.L.C.*, 126 S. Ct. 1837, 1839 (2006); 35 U.S.C. § 283 (2000). And preliminary injunctive relief is available against Nolicense Inc., if Genentech can demonstrate it is likely to succeed on the merits. Beyond that, Nolicense Inc. faces the prospect of damages for infringement, which (especially given the threat

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[2] For simplicity, this brief will refer throughout to challenges based on invalidity, and presume the principles developed here apply with equal force whether the legal argument against the patent owner is premised on validity, enforceability, or scope of the patent (i.e., non-infringement).

of treble damages) will almost certainly exceed what it would have paid had it negotiated a royalty with Genentech in the first place. 35 U.S.C. § 284 (damages must be "adequate to compensate for the infringement, but in no event less than a reasonable royalty . . . together with interest and costs as fixed by the court").

Nolicense Inc.'s second option is to desist from using the patented invention and file a declaratory judgment action challenging the patent's validity. Here, Nolicense Inc. does not face the threat of an injunction or treble damages, but only because it has chosen to forego the business advantage of using the invention while the litigation sorts out the parties' respective rights.

At the end of the day, under either scenario, if Nolicense Inc. is found to be wrong on the merits, it will have a price to pay for fruitlessly attacking Genentech's patent. Genentech may choose not to grant a license to Nolicense Inc., or if it does, it may set the price to include a litigation premium. No patent owner in Genentech's position would offer Nolicense Inc. the same royalty it would have offered had Nolicense Inc. embarked on a non-adversarial license negotiation from the start, instead of suing or inviting a litigation by infringing.

***The repudiating licensee's dilemma.*** Renounce Co. takes a different route but ultimately faces the same hard choices as Nolicense Inc. It secures a license from Genentech after negotiating a suitable royalty. It then has second thoughts, and challenges the premise of the contract—that Genentech has a valid and enforceable patent and that Renounce Co.'s use would infringe that patent. To do so, it renounces the contract, and stops paying royalties. Genentech, obviously, will expect and demand that Renounce Co. stop using the patented invention.

At this point, Renounce Co. faces the same resist-or-desist dilemma as Nolicense Inc., with the same ramifications. If Renounce Co. continues to use the invention as it did while the license was operative,

Genentech can seek preliminary and permanent injunctive relief and assert claims for treble damages as well. *See Cordis Corp. v. Medtronic, Inc.*, 780 F.2d 991, 995 (Fed. Cir. 1985) ("At present, plaintiffs already have the option of withholding royalties and thereby breaching the licensing agreement; of course, they would then run the risk of an injunction if they should lose on the merits." (quoting *Warner-Jenkinson Co. v. Allied Chem. Corp.*, 567 F.2d 184, 188 (2d Cir. 1977)). Renounce Co. can avoid these unpleasant consequences only by desisting from any further use of the invention, though its business might suffer from such a voluntary choice.

Either way, Renounce Co., like Nolicense Inc., is taking a calculated risk. If it does not prevail on its bid to invalidate the underlying patent, Genentech might respond by refusing to grant another license to a party that has already renounced one contract. If Genentech does grant a license, it will undoubtedly decline to offer Renounce Co. the same price it negotiated before Renounce Co. reneged and sued. Genentech will demand a litigation premium.

***Free pass for the licensee in good standing.*** Licensue Co. is shrewder than both Nolicense Inc. and Renounce Co. Discomfited with the difficult choices, burdens, and risks the other two companies face, Licensue takes a different tack. Like Renounce Co., Licensue approaches Genentech and negotiates a license to use the patented product and then turns around and files a lawsuit alleging that the patent is invalid. But unlike Renounce Co., Licensue does not repudiate the contract. It opts instead to challenge the premise of the contract—that Genentech has a valid patent to license—while clinging to its benefits under the contract.

In order to enter into a licensing contract, the two companies had negotiated a royalty (just like Renounce Co. did). Maybe Licensue Co. challenged the patent's validity in the course of negotiations, in which case Genentech may well have discounted the royalty to ensure patent peace. *See MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376, 1378

(Fed. Cir. 2005), *pet. for cert. filed* (in a parallel case, MedImmune signed a license agreement after arguing that the patent was invalid and its activities were noninfringing, and sued the next year). Maybe Licensue Co. stood mute about such claims, intending to ambush Genentech with them, or to raise them only if the product was a sensation and royalty payments mounted. Either way, the royalty is set at a rate that both parties at the outset agree is fair. Genentech does not tack on a litigation premium, of course, because it does not anticipate betrayal.

With an executed license agreement in its pocket, Licensue Co. has secured a contractual right to use the invention for the royalty negotiated. The right is secure even if Genentech's patent increases in value, even if Licensue's product is a sensation beyond everyone's wildest imagination, and even if Genentech has second thoughts about whether Licensue deserves the license. When Licensue Co. sues Genentech, without repudiating the contract, it insists on enforcing its contractual right to continue exploiting the invention. If Genentech tries to revoke the license, Licensue cries, "Breach of contract." If Genentech tries to adjust the royalty, in light of changed circumstances, Licensue responds, "We have a deal." If Genentech tries to sue for infringement, Licensue wins a dismissal with the simple defense, "We have a license." *See Spindelfabrik Suessen-Schurr, Stahlecker & Grill GmbH v. Schubert & Salzer Maschinenfabrik Aktiengesellschaf.*, 829 F.2d 1075, 1081 (Fed. Cir. 1987) ("[A] patent license agreement is in essence nothing more than a promise by the licensor not to sue the licensee.").

Through its treachery, Licensue averts all the dilemmas and burdens that Nolicense Inc. and Renounce Co. face. All three companies are challenging the patent's validity. But Licensue, unlike the others, retains an unassailable right to continue using the invention while the litigation unfolds. Only Licensue can use the patented invention with no fear of paying more in damages than the royalty would require, and,

of course, Licensue is immune from any possibility of treble damages. Licensue, alone, has locked in a license and a royalty that is guaranteed, even if its claims of invalidity are rejected. Licensue is the only one that has managed to insulate itself from a litigation premium if its litigation fails. In short, if Licensue is permitted to pursue this path, it has essentially cloaked itself in an immunity that Genentech never intended to sell, and can challenge the patent unburdened by any negative consequences or hard choices. Pet. 3 (MedImmune admits that it pursued this strategy because it was "unwilling to risk crippling infringement judgments, with possible consequences of injunction, treble damages and attorneys' fees").

**B. It Is Unfair to Allow a Licensee to Sue While Retaining the Benefits of the License.**

That is unfair.

It would be unfair, and (for policy reasons described later, *see infra* Point II.C) unwise, to give licensees such latitude for licenses they enter into in the future. But it is doubly unfair to allow a company like Licensue to get away with such duplicity in connection with existing contracts. Existing contracts were negotiated with the expectation, on both sides of the table, that such a maneuver would be impermissible.

Well before the Federal Circuit concluded that this sort of suit could not proceed for lack of subject matter jurisdiction, *see Gen-Probe, Inc. v. Vysis, Inc.*, 359 F.3d 1376, (Fed. Cir.), *cert. dismissed*, 543 U.S. 941 (2004), it had held that, as a matter of equities, a licensee must choose between enjoying the benefits of the license and challenging the patent. More than two decades ago—before the issuance of any patent that remains in force today—the Federal Circuit observed that "a licensee [may] cease payments due under a contract while challenging the validity of a patent," but it may "*not* . . . avoid facing the consequences that such an action would bring." *Cordis,* 780 F.2d at 995 (emphasis

in original). Just three years later, the Federal Circuit held, again as a matter of equity, that "despite the public policy encouraging people to challenge potentially invalid patents, there are still circumstances in which the equities of the contractual relationships between the parties should deprive one party . . . of the right to bring that challenge." *Diamond Scientific Co. v. Ambico, Inc.*, 848 F.2d 1220, 1225 (Fed. Cir.), *cert. dismissed*, 487 U.S. 1265 (1988). In that particular case, the court held that an assignor could not assign a patent, collect full payment for the property, and then infringe on the ground that the patent it sold was worthless.[3] Equitable principles prohibit the perfidy.

Any conceivable doubt about how these principles apply to a Licensue (or a MedImmune) the Federal Circuit put to rest nearly a decade ago, when it held that "a licensee . . . cannot," consistent with equitable principles, challenge the validity of a patent "until it (i) actually ceases payment of royalties, and (ii) provides notice to the licensor that the reason for ceasing payment of royalties is because it has deemed the relevant claims to be invalid." *Studiengesellschaft Kohle m.b.H. v. Shell Oil Co.*, 112 F.3d 1561, 1568 (Fed. Cir.), *cert. denied*, 522 U.S. 996 (1997).

At least since then, both licensors (like Genentech) and licensees (like MedImmune or Licensue) entered into these contractual agreements knowing that the licensee could not cling to the contractual benefits while challenging the patent. Licensors in Genentech's position had no reason to insinuate

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[3] The court distinguished this assignor situation from a situation of a "licensee, who . . . [is] *forced to continue to pay* for a potentially invalid patent" while being denied the right to challenge the patent's validity. *Diamond*, 848 F.2d at 1224 (emphasis added). That is the situation addressed in *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969), which, as is demonstrated below, is distinguishable from the Licensue situation (and the situation here) where the licensee wants to retain the license *and* challenge the patent's validity.

additional protections into their contracts and no need to adjust royalty rates or payment terms for the possibility that an insidious licensee might seek to challenge the very premise of the contract without relinquishing the contract's benefits.

If a company like Licensue (or MedImmune) is permitted to challenge the patent while retaining the benefits of the contract, then every one of the thousands, even millions, of licensees across the spectrum of industries can do the same. Contracts collectively totaling hundreds of millions of dollars in value will be unsettled. With no disincentive to sue, licensees would have every reason to seek better deals than the ones they struck, whether the deal was struck 15 days ago or 15 years ago. They would begin with licenses that have yielded the greatest commercial success, reallocating, with the unfair benefit of 20/20 hindsight, the valuation and risk assessments the parties themselves agreed upon.

In fact, any alternative rule would affirmatively encourage unscrupulous behavior. If Licensue's behavior were permissible, a company like Nolicense Inc. or Renounce Co. would have every reason to mimic it. Businesses would face irresistible financial incentives to negotiate a quick deal authorizing the use of the patented invention while harboring the secret intention of filing a lawsuit without risk the moment the deal is inked, or once the royalty payments escalate.

## II. A LICENSEE WHO RETAINS THE BENEFITS OF A CONTRACT IS EQUITABLY ESTOPPED FROM SUING IN DEROGATION OF THE CONTRACT.

Granted, not every unscrupulous business practice is impermissible, and cries of unfairness rarely suffice to derail a lawsuit. But in the context of a declaratory judgment suit like this one, equitable and public interest principles control,

and, for all the reasons described in Genentech's and the City of Hope's briefs, these principles can and do preclude courts from taking jurisdiction at the outset of litigation. For centuries, courts here and in England have enforced the rule that a party to a contract in MedImmune's position cannot challenge the validity of any underlying property interest without relinquishing the benefits conveyed. *See infra* Point II.A. Far from abolishing that rule in *Lear*, this Court's analysis reinforces it, both as a matter of equity, *see infra* Point II.B, and as a matter of the public interest, *see infra* Point II.C.

### A. Under Traditional Equitable Principles, a Licensee Cannot Simultaneously Retain the Benefits of a Contract and Act in Derogation of the Contract.

"You can't have your cake and eat it too" is more than just a tired saw. It is an axiom of equity with a common law pedigree almost as ancient as the aphorism itself. Under traditional principles of equity, MedImmune would not be able to claim the benefits of its contract and at the same time challenge the validity of the patent on which the contract is premised.

This common law principle of equity predates the Republic.[4] Two centuries ago, an English court encountered

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[4] *See, e.g., Lewis v. Willis*, (1752) 1 Wils. K.B. 314, 314, 95 Eng. Rep. 637, 637 (a tenant's challenge to a landlord's title to the leased property is a bad plea to an implied promise to pay on the use and occupation of land); *Cooke v. Loxley*, (1792) 5 T.R. 4, 4, 101 Eng. Rep. 2, 3 (K.B.) ("Generally speaking, a man ought not to be suffered to object to the illegality of a contract into which he has solemnly entered[.]"); *Phipps v. Schulthorpe*, (1817) 1 Barne. & Ald. 50, 53, 106 Eng. Rep. 19, 20 (K.B.) ("[B]eing once a tenant, it is not competent to [the defendant] to dispute his landlord's title."); *Fleming v. Gooding*, (1834) 10 Bing. 549, 550-51, 131 Eng. Rep. 1008, 1008 (C.P.) ("[I]t is not open to the tenant to dispute the title of the . . . landlord. . . . The rule of estoppel prevails."); *Agar v.*

a contracting party who attempted the same ploy MedImmune tried here. *See Balls v. Westwood*, (1809) 2 Camp. 11, 170 Eng. Rep. 1064 (K.B.), *overruled on other grounds by Mountnoy v. Collier*, (1853) 1 E. & B. 630, 639-40, 118 Eng. Rep. 573, 577 (*Mountnoy* declared only that a tenant could assert as a defense that his landlord's title had expired since the lease began, not that it was invalid when leased). The contract in *Balls* was a lease, and the tenant was trying to challenge the landlord's title to the property while simultaneously enjoying the benefits of the contract by occupying the premises. Lord Ellenborough asked the tenant: "Did you by any formal act renounce the [landlord's] title? Did you divest yourself of the possession you obtained under the [landlord], and commence a fresh holding under another person?" *Id.* at 12. When the tenant answered no, the court, incredulous at the duplicity, thundered: "You may as well attempt to remove a mountain. You cannot controvert the continuance of the title under whose demise you continue to hold." *Id.*

For almost as long as there have been American courts, our jurisprudence has been equally hostile to similar efforts, at times echoing Lord Ellenborough's admonishment about removing mountains. *See Tilyou v. Reynolds*, 15 N.E. 534, 537 (N.Y. 1888) (recounting the exchange). Our courts have uniformly hewn to the view that a party who enjoys a contract to use or occupy property cannot simultaneously retain the property *and* challenge the property owner's rights. *See, e.g., Vernam v. Smith*, 15 N.Y. 327 (1857). From the days of Chief Justice John Marshall, this Court has followed the rule, observing that estoppel applies where

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*Young*, (1841) Car. & M. 78, 80, 174 Eng. Rep. 417, 418 (Nisi Prius) ("[T]he principle of law is, that a tenant having taken of his landlord shall not deny his landlord's title, because, if he has taken land from a person who had no right to give it, his first duty is to surrender it back, not to deny the title of the donor or lessor.").

there is a landlord-tenant relationship *and* the tenant continues to retain possession of the property. *See Willison v. Watkins*, 28 U.S. (3 Pet.) 43, 47-48 (1830) (declining to apply estoppel in that case because the tenant had long since "terminated the tenancy" by renouncing the lease, which put the landlord on notice that the tenant "meant to hold from that time by his own title and on adverse possession"); *Rector v. Gibbon*, 111 U.S. 276, 284 (1884) (holding that tenants, "while retaining possession, are estopped to deny [the landlord's] rights"); *cf. Blight's Lessee v. Rochester*, 20 U.S. (7 Wheat) 535, 547 (1822) (discussing the scope of the estoppel doctrine). Lower courts in this country faithfully applied the rule as well. As one court long ago put it, "[t]he foundation of the estoppel is the fact of the one obtaining possession and enjoying possession by the permission of the other." *Tilyou*, 15 N.E. at 536. "[S]o long as one has this enjoyment he is prevented by this rule of law from turning round and saying his landlord has no right or title to keep him in possession." *Id.*

While the doctrine sprouted from the landlord-tenant context, the courts considered the principle universally applicable to all manner of property rights and contractual relationships. As then-Judge Cardozo observed almost a century ago, the principle "applies with equal force to a licensee in possession of land as against his licensor, and to other relations." *Farnsworth v. Boro Oil & Gas Co.*, 109 N.E. 860, 862 (N.Y. 1915) (Cardozo, J.); *see also City of Jamestown v. Pa. Gas Co.*, 1 F.2d 871, 880-81 (2d Cir. 1924). Judge Cardozo was addressing a contract that arose from a natural gas supplier's request for permission to lay gas lines across a highway to supply gas to the town's inhabitants. The town board agreed to grant this privilege in exchange for the gas company's promise to cap the price of gas sold to the town's inhabitants. Fourteen years later, the gas company increased its rate beyond the agreed-upon cap. When challenged, the gas company claimed that the original deal was a nullity because it never needed the town's

permission to lay pipes in the first place. Drawing upon the earlier landlord-tenant cases, the court held that the gas company was "estopped to deny the binding force of its agreement." *Farnsworth*, 109 N.E. at 861. Judge Cardozo noted that the defendant was not permanently barred from asserting its legal position about the town's property rights: "When the defendant takes up its mains and vacates the highway, a court will listen with some tolerance to its plea that it has been there without right." *Id.* at 863. But as long as the company was retaining the benefits of the contract, judicial tolerance was in short supply.

It was not long before the courts encountered similar scenarios in the context of intellectual property rights, and continued to apply the time-tested equitable rule there, too. *See Westinghouse Elec. & Mfg. Co. v. Formica Insulation Co.*, 266 U.S. 342, 350 (1924) (analogizing estoppel rules in a situation where "one lawfully conveys to another a patented right to exclude the public from the making, using and vending of an invention" to the estoppel rules that would apply to "a grantor of a deed of land" who "impeach[es] the effect of his solemn act as against his grantee"); *Taylor v. Hare*, 1 Bos. & Pu. (N.R.), (1805) 259, 262, 127 Eng. Rep. 461, 462 (C.P.) (applying equitable principles to deny recovery in patent case, where the licensee "has had the enjoyment of what he stipulated for"); *Wilder v. Adams*, 29 F. Cas. 1216, 1217 (D. Mass. 1846) (rejecting patent invalidity as a defense to a claim of nonpayment of royalty). Thus, the rule was that a "licensee under a patent cannot assail it as void while manufacturing under its protection . . . until his license has been surrendered or withdrawn, and his act can be treated as an infringement." *Saltus v. Belford Co.*, 31 N.E. 518, 519 (N.Y. 1892); *see Edison Gen. Elec. Co. v. Thackara Mfg. Co.*, 31 A. 856, 857 (Pa. 1895) ("[W]hile . . . the licensee is enjoying the benefit of [the patent's] supposed validity, he is bound to pay the stipulated royalty, and cannot set up as a defense the actual invalidity of the patent[.]"). There, as in the other areas, some courts made clear that a

licensee was not forever barred from challenging the validity of the licensor's property right, just because it once took a license. Those courts recognized that the challenge could not proceed unless the licensee repudiated the contract (putting itself in the Renounce Co. rubric). *See, e.g., Marston v. Swett*, 82 N.Y. 526, 534 (1880) (licensees cannot contest validity of the patent "'until they can show that the patent has been rescinded or revoked, or that notice has been given to the [licensor] that the [licensees] will not pay any more under the contract'"). The licensee would not have to take a step as extreme as exhuming gas mains from under a highway, but it would have to do the intellectual property equivalent of vacating the premises: provide unequivocal notice of its intention to renounce the license's protection and thus proceed as a potential infringer—a trespasser on the challenged intellectual property rights. *Compare Skinner v. Walter A. Wood Mowing & Reaping Mach. Co.*, 35 N.E. 491, 492-93 (N.Y. 1893), *L. Heller & Son v. Lessner Co.*, 212 N.Y.S. 175, 178-79 (N.Y. App. Div. 1925), *and Bucky v. Sebo*, 95 N.Y.S.2d 769, 771 (N.Y. App. Div. 1950), *with Willison*, 28 U.S. (3 Pet.) at 48.

This Court eventually took the estoppel position quite a bit further—further than the original common law cases would have gone. In what the Court in *Lear* called the *Hazeltine* rule, this Court held that once a licensee entered into a license premised upon the existence of a valid patent, the licensee was estopped from challenging the validity of the patent forever. *See Automatic Radio Mfg. Co. v. Hazeltine Research, Inc.*, 339 U.S. 827, 836 (1950). In *Hazeltine*, the Court estopped the licensee from challenging the patent, even though it was unclear whether the licensee actually repudiated the license, or needed to repudiate when it did not practice the licensed patents. Thus, after *Hazeltine*, even if the licensee repudiated the contract, and foreswore the benefits, it still could not challenge the patent. Under the *Hazeltine* rule this Court embraced, even Renounce Co. would be barred from challenging a patent's validity. The

only sort of business that could ever challenge a patent was one (like Nolicense Inc.) that had never entered into a license tacitly acknowledging the patent's validity.

In the ensuing years, this Court began retreating from this musclebound version of estoppel, carving out various exceptions to its own more expansive rule that a company like Renounce Co. was forever estopped from suing. *See Lear, Inc. v. Adkins*, 395 U.S. 653, 663-67 (1969) (recounting the progression of cases).[5] Never once, however, did this Court suggest that it was prepared to retrench on the core common law principle—that a licensee who wanted to challenge a patent would still have to renounce.

### B. This Court's Analysis in *Lear v. Adkins* Confirms that Equitable Principles Preclude this Suit.

This Court did nothing to change the baseline rule in *Lear v. Adkins*, 395 U.S. 653 (1969), either. Rather, *Lear* held that the Court would no longer adhere to the more expansive position. *Lear* held that licensee estoppel would no longer apply in one category of cases involving licensees—cases where a licensee (like Renounce Co.) *repudiates* the license. Thus, *Lear* overruled the *Hazeltine* rule, under which a licensee was estopped from repudiating a license to challenge a patent's validity. But *Lear* did not "remove [the] mountain" Lord Ellenborough imagined; it

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[5] Notably, none of the cases in either mode—the more expansive rubric or the retrenchment mode—involved a declaratory judgment action. They all presented circumstances where a licensor sued to enforce the license agreement. *See, e.g., United States v. Harvey Steel Co.*, 196 U.S. 310, 313 (1905) ("This is a claim for royalties upon a contract made between the parties to the suit[.]"); *Kinsman v. Parkhurst*, 59 U.S. (18 How.) 289, 291 (1856) (suit to enforce promise not to manufacture patented machines after a certain period of time).

said nothing to undermine the continued vitality of the longstanding estoppel doctrine as it relates to a case, like this one, where the licensee (like MedImmune or our hypothetical Licensue Co.) refuses to repudiate and tries to challenge the basis of the license while retaining all the license's protections. In fact, *Lear*'s analysis only confirms that the equitable principles survive in this context.

**1. *Lear* focused on the equities relating to a repudiating licensee.**

*Lear* presented the classic Renounce Co. fact pattern. An inventor (Adkins) licensed an invention to a licensee (Lear), while his patent application was pending. *Id.* at 657-58. They negotiated a royalty. *Id.* at 657. Before the patent was even issued, the licensee concluded that the invention was not patentable. *Id.* at 659-60. The licensee *renounced the license*, and stopped paying royalties. *Id.* at 659. The inventor did, indeed, secure a patent and once the patent issued, the inventor sued to collect the royalties owed under the contract. *Id.* at 660. The licensee defended on the ground that the patent was invalid, and the trial court agreed, ruling that the "invention had been completely anticipated by prior art." *Id.* The inventor invoked this Court's expansive version of licensee estoppel to preclude the licensee from acting in derogation of the contract. *Id.* at 661-62. The licensee responded "that a licensee may escape the impact of estoppel *simply by announcing that it has repudiated the licensing agreement.*" *Id.* at 662 n.10 (emphasis added).

The California Supreme Court agreed with the inventor, invoking "'one of the oldest doctrines in the field of patent law.'" *Id.* at 656 (quoting 67 Cal. 2d 882, 891 (1967)). Notably, the state court articulated the narrower version of that estoppel doctrine: "'[S]o long as a licensee is *operating under a license agreement* he is estopped to deny the validity of his licensor's patent in a suit for royalties under the agreement.'" *Id.* (quoting 67 Cal. 2d at 891) (emphasis added).

Far from addressing every conceivable application of this rule, this Court addressed the narrower question, whether "the doctrine of estoppel ... bar[s] Lear from proving that Adkins' ideas were dedicated to the common welfare by federal law" under the category of circumstances presented there—where the licensee was no longer seeking the benefits of the license. *Id.* at 662. This Court made clear that it was not reaching a categorical conclusion as to every application of estoppel against a licensee in all the circumstances where estoppel had historically been sustained. Rather, the Court identified two separate categories of situations, each involving a licensee who "*repudiate[s] his promises*," *id.* at 668 (emphasis added)—i.e., a *former* licensee, like Renounce Co.—with several variations of each category:

***Category I:*** "The most typical situation in which patent licenses are negotiated," where the licensor obtains the patent first and then licenses it to the licensee, who proceeds to repudiate the contract—

***(A)*** ... and the licensor originally obtained the patent through fraud. *Id.* at 669-70.

***(B)*** ... and the patent was not fraudulently obtained, but is challenged on some other ground. *Id.* at 670.

***Category II:*** The "far more complicated" scenario where the licensor licenses the invention before obtaining the patent—

***(A)*** ... and the licensor claims that estoppel compels the licensee to pay a royalty for the duration of the contract, even after the patent is found invalid. *Id.* at 671-72.

***(B)*** ... and the licensor claims that estoppel compels the licensee to continue paying the contractual royalty during the pendency of the litigation. *Id.* at 673.

> ***(C)*** . . . and the licensor asserts that estoppel compels the licensee to pay royalties at least for the period before the patent was issued. *Id.* at 674.

The Court worked through each scenario, one by one, assessing the equities separately as to each. For each, the goal was to "accommodate the competing demands of the common law of contracts and the federal law of patents." *Id.* at 668. "On the one hand," the Court observed, "the law of contracts forbids a purchaser to repudiate his promises simply because he later becomes dissatisfied with the bargain he has made." *Id.* Against this interest, the Court balanced "the important public interest in permitting full and free competition in the use of ideas which are in reality a part of the public domain." *Id.* at 670. As to each scenario, the Court "reconsider[ed] on their own merits the arguments which may be properly advanced on both sides of the estoppel question." *Id.* at 668.

The Court found some of the balances fairly straightforward. For example, it was "difficult to perceive why good faith requires" much solicitude of the contract rights "of the licensor who has obtained his patent through a fraud on the Patent Office" (Subcategory I(A)). *Id.* at 669-70. The balancing act for Category II, however, presented "a far more complicated estoppel problem." *Id.* at 671. One variation on this category—Subcategory II(C)—presented a problem that was so "much more difficult" that the Court declined to resolve it, or even to "attempt to define in even a limited way" the parameters of a solution. *Id.* at 674-75.

Ultimately, as to each subcategory that the Court did grapple with, it ended up concluding that the equities tilted in favor of protecting the federal interest in permitting the challenge to continue. Accordingly, the Court, overruled the expansive *Hazeltine* rule in each of those contexts. *Id.* at 656, 671. For each, the Court sought "to balance the claims of promisor and promisee in accord with the requirements of good faith." *Id.* at 670. The key to the balance in each case was the observation that "[l]icensees may often be the only

individuals with enough economic incentive to challenge the patentability of an inventor's discovery," and the concern about the loss to the public "*[i]f they are muzzled.*" *Id.* (emphasis added). The point in each context was that the licensee should be *freed* from the contractual obligations—that it should be permitted, in other words, to *repudiate* and sue—because if the licensee is "muzzled, the public may continually be required to pay tribute to would-be monopolists without need or justification." *Id.* What most concerned the Court was the prospect of "disabling *entirely* all those who have the strongest incentive to show that a patent is worthless." *Id.* at 672 (emphasis added). The Court expressed a secondary concern over the prospect of a rule that "would give the licensor an additional economic incentive to devise every conceivable dilatory tactic in an effort to postpone the day of final judicial reckoning" on the validity of the patent. *Id.* at 673.

To say, as MedImmune does, that *Lear* "abolished . . . licensee estoppel," Pet. 8, is like saying that *Roper v. Simmons*, 543 U.S. 551 (2005), abolished the death penalty. *Lear* abolished the defense for licensees that repudiate the license (or at least most of them); it largely abolished what might be called "*former* licensee estoppel," *Hazeltine's* extension of the traditional common law rule. But it said nothing at all about "current licensee estoppel" or estoppel as it relates to licensees in good standing who are not willing to renounce their licenses. Nor did it say anything about the traditional common law rule that required patent licensees to repudiate before challenging validity. *See* William C. Rooklidge, *Licensee Validity Challenges and the Obligation to Pay Accrued Royalties: Lear v. Adkins Revisited* (pts. 1, 2 & 3), 68 J. Pat. & Trademark Off. Soc'y 506 (1986), 69 J. Pat. & Trademark Off. Soc'y 5, 63 (1987), pt. 1 at 515-16 ("The early patent cases recognized that a licensee could avoid application of the bar against validity challenged by repudiating the license agreement."). In fact, in *Lear*, the licensee "'concede[d] that it would be estopped to contest

the validity of any patent issued to [the licensor] so long as it continued to operate under that agreement.'" 395 U.S. at 679 n.1 (White, J., concurring). That is this case.

**2. Under *Lear's* analysis, the equities prohibit a suit by a licensee in good standing.**

As to a licensee who does "continue[] to operate under" the license, and declines to repudiate the license—the scenario represented by this case and by our hypothetical Licensue Co.—the balance of interests comes out the other way, just as the licensee conceded. On the one hand, as demonstrated above, the equities weigh more heavily in favor of the licensor in this context. *See supra* Point I. On the other hand, faithful application of traditional equitable rules against a licensee who has not repudiated the contract does not in any way "muzzle" the licensee, 395 U.S. at 670, or "disabl[e]" the licensee "entirely," *id.* at 672. The licensee is as free as anyone else to challenge the patent. All the licensee has to do is repudiate the contract. Imposing this requirement on the licensee does not create any perverse incentives for the licensor to prolong the litigation through "dilatory tactic[s]." *Id.* at 673. From the patent owner's perspective, the former licensee is now like any other challenger to a patent, whether the former licensee infringes, inviting the patent owner to sue, or files a declaratory judgment action.

This is the point MedImmune misses when it argues that faithful application of equitable estoppel rules to this case would put it, and other licensees, to an untenable "Hobson's choice"—a choice between retaining the contractual benefits it enjoys and rolling the dice on unpredictable patent litigation, with all the attendant risks, including the possibility of treble damages and an injunction. Pet. Br. 45. The traditional equitable estoppel rule does not put MedImmune to that choice; the Patent Act does. *See* 35 U.S.C. § 284 (2000). As the Federal Circuit observed, in response to this very argument, "[e]very potential infringer who is threatened with suit, or who is sued, for patent

infringement must decide whether to settle or fight." *MedImmune, Inc. v. Centocor, Inc.*, 409 F.3d 1376, 1382 (Fed. Cir. 2005), *pet. for cert. filed.* Our hypothetical Nolicense Inc. and Renounce Co. both face that choice—and can hardly complain that the choice is against federal policy. The same goes for MedImmune's concern that it simply must continue using the patented invention, and worries about being enjoined. Again, every company that wishes to (or has a business need to) use a patented invention could say that same thing. Nothing in the Patent Act, or federal patent policy, requires a court to shield an infringer from an injunction, from damages, or from the threat of treble damages. To the contrary, such a shield would only detract from the structure of the Patent Act.

Put another way, federal policy does not override the statutory rule that a nonlicensee (Nolicense Inc.) or a repudiating licensee (Renounce Co.) must make the hard choice between foreswearing use of the invention or infringing. Nor does federal policy override the statutory rule that any company that opts to infringe during the litigation faces the risk of an injunction and treble damages—whether or not the infringer once entered into a license. It would be a perverse form of federal policy that would override those same statutory policies for an infringer who negotiates a deal and reneges on it, but insists on retaining the benefits.

### C. A Rule Incentivizing Parties to Secure Licenses and Then Sue Is Against the Public Interest.

*Lear*'s analysis turned not just on equities but on broader questions of public policy—questions about what legal rule would most fulfill the goals of the Patent Act. Thus, the appropriate legal rule in this context cannot be determined without an assessment of the public policy implications.

The Patent Act represents an intricate balance. On one side of the balance is the interest *Lear* emphasized—the

interest in ensuring "that all ideas in general circulation be dedicated to the common good unless they are protected by a valid patent." 395 U.S. at 668. That interest is advanced by ensuring that those who have the greatest incentive to challenge invalid patents are not "muzzled." *Id.* at 670. On the other side of the balance, of course, is the most common justification for awarding patents, to encourage innovation by allowing those who innovate to reap the profits of the innovation. *See Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 63-64 (1998). While it is important to ensure that invalid or questionable patents are not unduly and artificially insulated from challenge, the public interest is not served by a regime that encourages meritless or dubious challenges to valid patents. Such challenges erode the rewards that genuine innovators reap and do not materially advance the interest in releasing technology to the common good.

Further, society has an especially strong interest in encouraging patent holders to license patents that are valid, for a license advances both sides of the balance. On the one hand, licensing fees are among the most important rewards that a patent owner garners from a valid patent. On the other hand, only if a patent owner is inclined to license the patent will society reap the greatest utility from a patented invention. We must be wary of rules that will have the unintended effect of discouraging patent owners from licensing their inventions, or increasing the costs of licenses—whether in terms of increased royalties or increased transaction costs.

That is exactly what will happen in a regime in which licensees are free to challenge patents while retaining all the benefits of the license. The ramifications will be profound both for existing licenses and for future licensing practices.

We have already touched upon the effects of such a regime on licenses already granted. *See supra* Point I.B. Those licenses were negotiated with the assumption that they would have to terminate if the licensee later opted to challenge the patent. Licensors did not have to specify that

condition in the license any more than they had to specify that a breach by the licensee would entitle the licensor to revoke the license. Whether the negotiation was explicit or not, the royalty reflects the value of that condition for both sides. It reflects the royalty discount a licensor was willing to offer in return for the licensee's willingness to relinquish (albeit perhaps temporarily) any challenges to validity, enforceability, or scope.

Reversing the unstated condition retroactively—like reversing the rule that a breach entitles the licensor to revoke the license—amends the deal that was struck. The result would be a systematic transfer of value from the licensor side of the ledger to the licensee. The transfer reforms the bargain struck in millions of contracts, many of which extend a decade or two into the future. (Consider, for example, a deal struck this past year that sets a royalty on an invention for which the patent is now pending.)

The impact of this rule change on future behavior will depend, in part, on whether a licensor and licensee could contract around the new rule. One would think that it would be permissible for a license to specify the understanding of the parties that, notwithstanding the suspension of licensee estoppel as a defense, the license will terminate if the licensee challenges the validity of the patent. That conclusion, however, is not at all clear. *Lear*, itself, invoked federal public policy to override explicit contractual terms. *See* 395 U.S. at 670-71; *see also Pope Mfg. Co. v. Gormully*, 144 U.S. 224, 235 (1891) (federal policy overrides contractual provision because the right to challenge a patent "is not only a private right to the individual, but founded on public policy"); *United States v. Glaxo Group Ltd.*, 410 U.S. 52, 57 (1973). And various circuits adhere to the rule that licensors cannot negotiate around the judicial estoppel rule that *Lear* adopted. *Kraly v. Nat'l Distillers & Chem. Corp.*, 502 F.2d 1366, 1369 (7th Cir. 1974) (no-challenge clause in a license agreement was unenforceable); *Massillon-Cleveland-Akron Sign Co. v. Golden State Adver. Co.*, 444

F.2d 425, 427 (9th Cir. 1971) (no-challenge provision in settlement agreement entered before litigation was filed was unenforceable). One court of appeals decision even goes as far as to hold that even an explicit understanding memorialized in a judicially approved settlement, is unenforceable. *Business Forms Finishing Serv., Inc. v. Carson*, 452 F.2d 70, 73-75 (7th Cir. 1971) ("[A] consent decree does not create an estoppel on the issue of validity.").[6] So licensors are unlikely to place much confidence in contractual fixes and will hedge their bets by behaving as if there can be no contractual protection.

How will patent owners do that? For starters, they will be less inclined to grant licenses. Under the current arrangement, a patent owner has an incentive to grant a license in the interest of protecting the patent from challenge. The more serious the challenge, or the greater the stakes for the patent owner, the sweeter the deal the patent owner would be willing to offer. *See Eureka Co. v. Bailey Co.*, 78 U.S. (11 Wall.) 488, 491 (1871) (a license is "an agreement manifestly intended to adjust conflicting rights"); Carl Shapiro, *Antitrust Limits to Patent Settlements*, 34 Rand J. Econ. 391, 392 (2003) ("Virtually every patent license can be viewed as a settlement of a patent dispute: the royalty rate presumably reflects the two parties' strengths or weaknesses in patent litigation in conjunction with the licensee's ability to invent around the patent."). The owner knows that the sweet deal does not legally insulate the patent from challenge entirely. But as long as the licensee must

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[6] On the other hand, the Federal Circuit has held that consent decrees and settlements are entitled to greater solicitude than negotiated contract terms. *See Foster v. Hallco Mfg. Co.*, 947 F.2d 469, 477 (Fed. Cir. 1991); *Flex-Foot, Inc. v. CRP, Inc.*, 238 F.3d 1362, 1368 (Fed. Cir. 2001). If that rule prevails, patent holders will feel obliged to engage in wasteful litigation as a prerequisite to obtaining an enforceable condition that could not be secured through direct negotiation.

relinquish the deal in order to challenge the patent, the patent owner can derive some comfort from offering the license. Should this Court declare that the patent owner can find no sanctuary whatsoever in a license—no matter how sweet the deal—patent owners will be less likely to offer deals, more likely to demand the full royalty up front (a term that could be prohibitively expensive for most licensees), and highly unlikely to offer discounts.

In fact, license prices will almost surely increase across the board. Under the current regime, a licensee who wages an unsuccessful challenge to a patent must return to the bargaining table if it wants to resume use of the invention. At that point, as is discussed above, the royalty will bear a litigation premium. *See supra* Point I.A. In essence, the licensee is forced to internalize some of the costs of its own frivolous or meritless challenge. Under the alternative regime, the licensor has no such outlet, for it is stuck perpetually with whatever price was negotiated up front. So if the licensor is ever going to cover the costs of litigation, those costs have to be reflected in the original royalty. The licensor has no choice but to treat every licensee as a potential patent challenger and to spread the litigation costs across all of them.

The difference is that the aggregate costs will be substantially higher than under the current regime. That is because there will inevitably be much more litigation under the alternative regime, and therefore much more litigation expense to distribute. Under the current rule, a licensee toying with the notion of suing has to repudiate the license which means the licensee now files a lawsuit challenging the patent only if the potential benefit of the lawsuit exceeds the value of the current license. Under the alternative regime, the licensee's cost-benefit analysis is simpler. Since the license will never be in jeopardy, the value of the license to the licensee will not be part of the cost-benefit analysis. So the lawsuit will materialize so long as the potential upside from the challenge (adjusted for the probability of success)

exceeds the costs of litigation. Lower disincentives to litigate spells more litigation.

It also spells more frivolous litigation. The licensee's current cost-benefit analysis filters out the weaker challenges. A rational licensee will not squander a valuable license without a conviction that the challenge is legally sound. Without the filter, the only barrier will be the cost of paying lawyers to bring weak claims.

If the federal policy were premised on the interest in proliferating challenges to patents, however frivolous, the alternative regime might be justified. But the federal policy is premised on the interest in encouraging *meritorious* challenges to *invalid* patents. So the current regime provides a much better fit to the interests this Court identified in *Lear*.

## III. THIS COURT SHOULD REACH THE ALTERNATIVE GROUND OF EQUITABLE ESTOPPEL, EVEN THOUGH THE COURT OF APPEALS' RULING WAS COUCHED IN JURISDICTIONAL TERMS.

If this Court were to conclude that the Court of Appeals' jurisdictional rule was incorrect, it should reach the alternative ground of equitable estoppel, for several reasons.

First, a remand for the lower courts to consider the outcome under equitable principles would be pointless, because the conclusion is foregone. The Court of Appeals has already ruled on the question. As we have seen, almost a decade ago the Federal Circuit definitively held that *Lear*'s rule suspending licensee estoppel does not extend to a case, like this one, where the licensee declines to repudiate the license. *Studiengesellschaft Kohle m.b.H. v. Shell Oil Co.*, 112 F.3d 1561, 1568 (Fed. Cir.), *cert. denied*, 522 U.S. 996 (1997); *see supra* Point I.B.

Even more recently, from the moment the Federal Circuit began treating the rule as a jurisdictional one, its analysis has been rooted as much in traditional principles of

equity and public interest—the very sorts of principles that infuse the equitable estoppel analysis—as in the language of jurisdiction. In *Gen-Probe*, for example, the Federal Circuit grounded its ruling in concerns that "permitting [the licensee in good standing] to pursue a lawsuit without materially breaching its license agreement yields undesirable results." *Gen-Probe Inc. v. Vysis, Inc.*, 359 F.3d 1376, 1382, (Fed. Cir.) *cert. dismissed*, 543 U.S. 941 (2004). One such concern was entirely equitable in nature: "[I]n this situation, the licensor would bear all the risk, while licensee would benefit from the license's effective cap on damages or royalties in the event its challenge to the patent's scope or validity fails." *Id.* A related point bespoke equally equitable concerns about good faith and fair dealing. The court observed that the licensor "voluntarily relinquished its statutory right to exclude by granting [the licensee] a . . . license. In so doing, [the licensor] chose to avoid litigation as an avenue of enforcing its rights." *Id.* The Federal Circuit evidently saw in this arrangement a reciprocal covenant on the licensee's part not to sue: "Allowing this action [by the *licensee*] to proceed would effectively defeat *those* contractual covenants . . . ." *Id.* (emphasis added). As a matter of public interest, the court noted that freeing licensees to retain the license and sue would "discourage patentees from granting licenses." *Id.*

Second, following *Gen-Probe*'s lead, the panel below, too, addressed the equities, and took note of the Declaratory Judgment Act's equitable framework. Pet. App. 7a. The Court of Appeals embellished upon the point the *Gen-Probe* court had made about "the inequity" in any alternative rule: "when the patent owner, having contracted away its right to sue, is in continuing risk of attack on the patent whenever the licensee chooses—for example, if the product achieves commercial success—while the licensee can preserve its license and royalty rate if the attack fails." *Id.* Enveloping its jurisdictional analysis in equitable garb, the Court of Appeals concluded that "[t]his imbalance distorts the

*equalizing principles* that underlie the Declaratory Judgment Act." *Id.* (emphasis added).

Third, a ruling by this Court reversing the dismissal on jurisdictional grounds, but not addressing the alternative equitable grounds for reaching the same result, could wreak commercial havoc and open the litigation floodgates. Emboldened by a ruling that signals free season on patent challenges, licensees will begin filing lawsuits challenging the validity or scope of the patents they have licensed. Unsure whether equity protects them where a jurisdictional rule does not, patent owners are bound to assume the worst, and adjust their licensing behavior as if they had no protection—refusing to license, demanding up front fees, or increasing royalties for all the reasons described earlier. *See supra* Point II.C.

Commerce thrives most where rules are certain. Whatever equitable rule this Court ultimately adopts, patent owners and licensees, alike, will be better off if this Court adopts that rule now.

## CONCLUSION

The Court should affirm the dismissal of this declaratory judgment action, whether on jurisdictional grounds or on alternative equitable grounds.

Respectfully submitted,

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IN THE

# Supreme Court of the United States

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MEDIMMUNE, INC.,
*Petitioner*,

v.

GENENTECH, INC., *et al.*,
*Respondents.*

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**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

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## BRIEF OF RICHARD L. DONALDSON, ROBERT B. LIESEGANG, SR., AND EMMETT J. MURTHA AS *AMICI CURIAE* IN SUPPORT OF RESPONDENTS

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## INTEREST OF *AMICI CURIAE*

*Amici* are licensing experts with extensive experience in negotiating, drafting, and reviewing all types of licenses and deal structures, especially those regarding patents.[1] Richard L. Donaldson worked at Texas Instruments for 31 years and was senior vice president and general patent counsel when he retired in 2000. He had the primary role in developing and implementing Texas Instruments' world-wide licensing programs in the semiconductor, calculator, and computer industries. Robert B. Liesegang, Sr. spent 18 years at IBM working on patent licensing issues, including serving six years as Director of Patent Licensing for IBM's Asia Pacific region until he retired in 2000. Emmett J. Murtha was IBM's Director of Licensing from 1981 to 1993, and was Director of Business Development from 1993 to 1997. He was President of the Licensing Executives Society in the 1999-2000 term.

All *amici* believe strongly in the importance of certainty and predictability in patent licensing agreements.

## INTRODUCTION AND SUMMARY OF ARGUMENT

The patent system is the primary way in which innovative ideas are translated into successful commercial inventions. That process of transformation starts with invention but in virtually all cases requires the use of licensing arrangements to complete it. The greater the success in licensing, the larger the return to individual patentees and the greater the spur to invention. Security of contract is essential to the successful use of all kinds of licensing arrangements.

This Court should affirm for two independent reasons. *First*, the Court should overrule or clarify *Lear v. Adkins*, 395

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[1] No counsel for a party authored this brief in whole or in part, and no person other than *amici curiae* and their counsel has made a monetary contribution toward its preparation or submission. All parties have consented to the filing of this brief by letters filed with the clerk.

U.S. 653 (1969), and make clear that private parties have the ability to contract with certainty in the patent licensing context. *Lear* prevents certainty in licensing. *Lear* preempts state contract law by allowing licensees to terminate their contracts and then contest the validity of licensed patents based on the theory that these challenges further the "strong federal policy favoring free competition in ideas which do not merit patent protection." *Id.* at 656. This analysis, however, overlooks two fundamental goals of patent law that the Court has recognized in later cases such as *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470 (1974) and *Aronson v. Quick Point Pencil Co.*, 440 U.S. 257 (1979): rewarding invention and encouraging disclosure. "Permitting inventors to make enforceable agreements licensing the use of their inventions in return for royalties provides an additional incentive to invention." *Aronson*, 440 U.S. at 262. *Lear* flies in the face of freedom of contract in commercial contexts.

*Second*, this Court should not adopt the rule proposed by MedImmune, which would extend the unsound rule in *Lear* by allowing a licensee to attack a patent without terminating the license. Under the rule in *Lear*, a licensee who wishes to attack the validity of the patent must first terminate the contract and forgo the benefit of the license. In other words, *Lear* requires the licensee to take a risk if it seeks to challenge a patent it has licensed. The licensee must either find some alternative invention to use in place of the patented technology or risk liability for patent infringement if it chooses to continue using that technology without a license. By allowing licensees simultaneously to pay the license royalty while attacking the license itself, the proposed rule would lead to a mushrooming of litigation and cause substantial unfairness to the licensor. Such a change also would harm most licensees by increasing royalty costs. The only licensees who will benefit are those such as MedImmune, who wish to undo their own voluntary bargains.

## ARGUMENT

### I. THIS COURT SHOULD OVERRULE OR CLARIFY *LEAR V. ADKINS*, 395 U.S. 653 (1969), TO ENSURE THAT PRIVATE PARTIES CAN BARGAIN WITH CERTAINTY IN LICENSING AGREEMENTS.

The procedural issues raised by Article III and the Declaratory Judgment Act offer this Court an easy way to affirm the decision below. Nevertheless, because of the enormous substantive importance of this issue, we urge this Court to use this case to ensure that private parties retain the maximum flexibility to structure their licensing transactions in the manner they deem best. The only way to achieve this end is to overrule or clarify *Lear v. Adkins*, 395 U.S. 653 (1969).

#### A. *Lear*'s Rationale is Inconsistent With This Court's Later Decisions

In *Lear*, this Court held that a licensee may terminate its license agreement at will in order to challenge the validity of the underlying patent. This ruling overturned the doctrine known as licensee estoppel, which had prevented a licensee from terminating a license agreement and thereby challenging the patent at issue in the contract. *See Automatic Radio Mfg. Co. v. Hazeltine Research, Inc.*, 339 U.S. 827, 836 (1950); *United States v. Harvey Steel Co.*, 196 U.S. 310, 316 (1905); *Kinsman v. Parkhurst*, 18 How. 289 (1856). Lear, the licensee, terminated the contract and stopped paying royalties to Adkins, the inventor, because Lear believed the patent was invalid. Adkins subsequently sued in California state court to enforce the contract, maintaining that Lear "was obliged to pay the agreed royalties regardless of the validity of the underlying patent." *Id.* at 656. The California Supreme Court ruled, as a matter of state contract law, that the doctrine of licensee estoppel applied and therefore barred licensees

from terminating their licenses and challenging the validity of the underlying patents. *See id.* at 663; *see also id.* at 673.

This Court granted certiorari in *Lear* to reconsider the issue of licensee estoppel in light of two decisions that it had just issued—*Sears, Roebuck & Co. v. Stiffel Co.*, 376 U.S. 225 (1964), and *Compco Corp. v. Day-Brite Lighting, Inc.*, 376 U.S. 234 (1964). *Lear*, 395 U.S. at 656. In *Sears* and *Compco*, the Court ruled that the policies inherent in federal patent law preempted a state's unfair competition law that imposed liability for "the copying of an article which is protected by neither a federal patent nor a copyright." *Sears*, 376 U.S. at 225. In sweeping language, the Court held that "[t]o allow a State by use of its law of unfair competition to prevent the copying of an article which represents too slight an advance to be patented would be to permit the State to block off from the public something which federal law has said belongs to the public." *Id.* at 231-32. A contrary rule would allow States to give "perpetual protection to articles too lacking in novelty to merit any patent at all under federal constitutional standards. This would be too great an encroachment on the federal patent system to be tolerated." *Id.* at 232. In *Lear*, this Court considered whether the *Sears/Compco* rationale of a "strong federal policy favoring free competition in ideas which do not merit patent protection," *Lear*, 395 U.S. at 656, meant that federal patent law impliedly preempted state contract law principles that prohibited patent licensees from challenging a patent's validity.

The Court in *Lear* held that "the federal law of patents" trumps "the common law of contracts." *Id.* at 668. It acknowledged that "[u]nder ordinary contract principles the mere fact that some benefit is received is enough to require enforcement of the contract, regardless of the validity of the underlying patent." *Id.* at 669. But in the Court's view, it was not "*unfair* to require a patentee to defend the Patent Office's judgment when his licensee places the question in

issue." *Id.* at 670 (emphasis added). Indeed, even as the Court specifically acknowledged that licensee estoppel was "consistent with the letter of contractual doctrine," it refused to enforce the plain terms of a contract because it decided that licensee estoppel was not "compelled by the *spirit* of contract law." *Id.* (emphasis added). Instead, the Court ruled that the "important public interest in permitting full and free competition" outweighed the terms of the contract negotiated between the parties. *Id.* Thus, using only some free-form notion of "public interest" loosely divined either from the Constitution itself or implicitly from the patent laws, the Court preempted settled state contract law and the "technical requirements of contract doctrine." *Id.*

*Lear* was a dramatic extension of *Sears* and *Compco*. Unlike those cases, *Lear* did not concern an effort under state law that in effect would expand patentable subject matter beyond what Congress authorized. Instead, it affected patents issued by the Patent and Trademark Office that were presumptively valid under federal law. *See* 35 U.S.C. § 282. This distinction gives rise to a very different set of concerns from those discussed by the Court in *Sears*, *Compco*, and *Lear*. For while one goal of patent policy is to provide a means to challenge invalid patents, another goal is to ensure that inventors can effectively exploit valid patents and therefore reap the rewards of their innovations. This fundamental incentive to invent is seriously skewed if licenses are under constant siege, with no assurance of finality. Later cases have recognized this point explicitly, and made clear that this Court will not find preemption in the patent context without addressing *all* of the objectives of patent law. Indeed, "[s]ubsequent case law" has made *Lear* "a legal anomaly" and has "undermined its basic legal principles." *Randall v. Sorrell*, 126 S. Ct. 2479, 2489 (2006) (plurality opinion).

In *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470 (1974), the issue was "whether state trade secret protection is pre-

empted by operation of the federal patent law." 416 U.S. at 472. The Court answered no: "The only limitation on the States is that in regulating the area of patents and copyrights they do not conflict with the operation of the laws in this area passed by Congress." *Id.* at 479. *See also Goldstein v. California*, 412 U.S. 546, 559 (1973) (refusing to find preemption of state law extending a copyright term). Unlike *Lear*, which found preemption of the common law of contracts based on "the strong federal policy favoring the full and free use of ideas in the public domain," 395 U.S. at 674, the Court in *Kewanee* noted two other primary objectives of patent law: "encouraging invention," and "disclosure, the quid pro quo of the right to exclude." 416 U.S. at 484.

The protection accorded to trade secrets by state law, the Court found, stimulated both invention and disclosure. Absent trade secret protection, the Court reasoned, "[t]he holder of a trade secret would not likely share his secret with a manufacturer who cannot be placed *under binding legal obligation* to pay a license fee or to protect the secret." *Id.* at 486 (emphasis added). "The result would be to hoard rather than disseminate knowledge." *Id.* Finally, the Court examined patent policy not only from the perspective of the holder of an invalid patent, as it did in *Lear*, but also from the perspective of patent owners who believe their inventions "meet the standards of patentability." *Id.* at 489. The *Kewanee* Court concluded by emphasizing the very features of patent law that should have led to the opposite result in *Lear*: efficiency in contracting, rewarding inventors, and congressional silence on the issue of preemption:

> Trade secret law promotes the sharing of knowledge, and the efficient operation of industry; it permits the individual inventor to reap the rewards of his labor by contracting with a company large enough to develop and exploit it. Congress, by its silence over these many years, has seen the wisdom of allowing the States to enforce trade secret protection. Until Congress takes

> affirmative action to the contrary, States should be free to grant protection to trade secrets.

*Id.* at 493.

Five years later, in *Aronson v. Quick Point Pencil Co.*, 440 U.S. 257, 258-59 (1979), the Court substantially undermined its stated rationale in *Lear* by holding that federal patent law does not preempt "state contract law so as to preclude enforcement of a contract to pay royalties to a patent applicant." The parties in *Aronson* negotiated a contract while the licensor's patent application was pending. The parties agreed that the licensee would pay a 5% royalty if the patent was granted and a 2.5% royalty if the patent application was not allowed within five years. *See id.* at 259. After the licensor failed to obtain a patent, the licensee attempted to renege on its contract. *See id.* at 260. It argued that federal patent law should preempt state contract law because the invention in *Aronson* was part of the public domain and *Lear* preempts those contracts that conflict with the "'the strong federal policy favoring the full and free use of ideas in the public domain.'" 440 U.S. at 261 (quoting *Lear*, 395 U.S. at 674).

This Court rejected the licensee's argument, and enforced the contract. The Court ruled that "[c]ommercial agreements traditionally are the domain of state law," *id.* at 262, and that "[o]ur holding in *Kewanee Oil Co.* puts to rest the contention that federal law pre-empts and renders unenforceable the contract made by these parties." *Id.* at 265. The Court examined all three goals of patent law it identified in *Kewanee*, not simply the single principle identified in *Lear* that ideas in the public domain should remain in the public domain. *See id.* at 262. The Court had little trouble finding that federal patent law did not preempt the contract because it judged the enforceability of the contract by focusing on the expectations of the parties at the time they made the agreement: "Permitting inventors to make enforceable agreements licensing the use of their inventions in return for royalties

provides an additional incentive to invention." *Id.* Moreover, the Court emphasized the importance of the contract itself, noting that "the parties resolved the uncertainties by their bargain." *Id.* at 264. The *Aronson* court summarily distinguished *Lear*, concluding that "neither the holding nor the rationale of *Lear* controls when no patent has issued, and no ideas have been withdrawn from public use." *Id.* Yet the result and reasoning of *Aronson* are quite inconsistent with *Lear*.

In *Bonito Boats v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 154 (1989), the Court further undermined *Lear* by specifically disapproving the "absolutist" language of *Sears* and *Compco* that was the very reason why the Court reconsidered the issue of licensee estoppel and its interaction with federal patent law. *See Lear*, 395 U.S. at 656. Rejecting the proposition that *Sears* stands for "a broad pre-emptive principle," 489 U.S. at 154, the Court in *Bonito Boats* stated that "our decisions since *Sears* have taken a decidedly less rigid view of the scope of federal pre-emption under the patent laws." *Id.* at 156. *Kewanee* and *Aronson*, the Court explained, show a "pragmatic approach" in deciding "the pre-emption of state laws dealing with the protection of intellectual property." *Id.*

### B. Under this Court's "Pragmatic" Preemption Analysis, *Lear*'s Policy Judgment Is Wrong

*Lear* overrode state laws of general applicability regarding the enforceability of contracts because of the Court's own judgment that federal patent law is inconsistent with finality and certainty in private licensing agreements. This assessment, however, is mistaken. A rule that enforces license agreements is in complete accord with federal patent policy and with this Court's preemption analysis. Rather, it is *Lear*'s broad rationale that is inconsistent with the "pragmatic" preemption approach adopted by this Court in post-*Lear* cases. *Bonito Boats*, 489 U.S. at 155.

Patent licensing agreements and exchanges today are of infinite variety. Patent owners may decide to license one patent for a set royalty rate. They might license a group of patents. They can agree to an exclusive or a non-exclusive license. They may decide to pool their patents, or engage in cross-licensing arrangements. They may donate their patents to a university, or commit to license a patent in order to join a standard-setting organization. Typically they use their patents as one part of a larger business transaction. *See generally* Mark A. Lemley, *Rational Ignorance at the Patent Office*, 95 Nw. U. L. Rev. 1495, 1500-08 (2001) (discussing some of the various ways patent owners use their patents). While the duration and price of the license are two standard terms, license agreements often contain literally dozens or even hundreds of clauses. "[T]he rise of patent portfolios in the business community has become so significant that portfolios have become the credo of firm value in the modern innovation environment." Gideon Parchomovsky & R. Polk Wagner, *Patent Portfolios*, 154 U. Pa. L. Rev. 1, 8-9 (2005). Licensing agreements are the critical mechanism by which parties exchange, share, and pool intellectual property rights. They mean little without certainty.

*Lear* does not further any of the goals of patent law that this Court identified in *Kewanee* and applied again in *Aronson*: encouraging invention, increasing disclosure, and allowing the public the full and free use of ideas in the public domain. *See Kewanee*, 416 U.S. at 484; *Aronson*, 440 U.S. at 262.

*First*, the *Lear* rule does not properly reward the inventor. As this Court stated in *Aronson*, "Permitting inventors to make enforceable agreements licensing the use of their inventions in return for royalties provides an additional incentive to invention." 440 U.S. at 262. The ability to bargain with certainty and create enforceable and predictable licensing agreements is central in properly incentivizing innovation.

The United States recognizes as much in its *amicus* brief on behalf of MedImmune, arguing that parties "may be able to" contract around any rule that increases uncertainty in licensing agreements, and identifying the means by which they may do so. Brief of United States as *Amicus Curiae* at 28. But the Government also acknowledges that the enforceability of the suggested provisions are "open question[s]" due to *Lear*. *Id.*

Moreover, the United States' alternatives are poor substitutes for a clear rule that would allow sophisticated parties to strike bargains in the manner they deem best. For example, the United States suggests that the parties could agree to a fully paid-up license in lieu of a contract specifying a reasonable royalty. Br. at 29. Such agreements, however, often are inefficient because they place an unquantifiable risk on one party or the other, frequently in a haphazard fashion. The patent holder who agrees to accept a lump-sum payment for a fully paid-up license runs the risk that the payment will prove to be inadequate if the licensor generates substantial revenues through exploitation of the patented invention. Similarly, the licensee risks paying a substantial sum of money for an invention that it might choose not to use or that may prove commercially unsuccessful. The government's suggestion of the up-front payment thus would compel parties to make inefficient agreements solely in an effort to work around unwanted public restraints on their freedom to contract as they see fit.

The United States itself made this very point in its *amicus* brief to this Court in support of the licensor in *Aronson*. *See* Brief for the United States as *Amicus Curiae*, *Aronson v. Quick Point Pencil Co.*, 440 U.S. 257 (1979) (No. 77-1413), 1978 WL 207171, at 8 ("At all events, a rule of law that would induce inventors to demand lump-sum payments, or payments spread over a short period, in order to be assured of adequate compensation for their ideas would not promote competition. It would simply require inventors and their

licensees to guess about what the idea would be worth."); *see also id.* at 22-24 & n. 10. An agreement with an ongoing royalty rate allows both parties to contract around this uncertainty by tying price to use. *Cf. In re Mahurkar Double Lumen Hemodialysis Catheter Patent Litigation*, 831 F. Supp. 1354, 1397 (N.D. Ill. 1993) (Easterbrook, J.) ("The actual market beats judicial attempts to mimic the market every time."). Consequently, it is likely that rules permitting flexibility in negotiation and contracting will result in a greater degree of licensing activity than a rule practically requiring parties to agree on a lump-sum amount as a licensing condition.

By imposing its own policy judgment in place of those of the parties and of the States, *Lear* "dramatically limit[s] the value of a patent, interfere[s] with efficient utilization of inventions and lead[s] to major resource allocation losses." John W. Schlicher, *Judicial Regulation of Patent Licensing, Litigation and Settlement Under Judicial Policies Created in* Lear v. Adkins, *in* 3 AIPLA Selected Legal Papers, No. 1 (1985); *see also* John W. Schlicher, *A Lear v. Adkins Allegory*, 68 J. Pat. & Trademark Off. Soc'y 427 (1986). Left to their own devices in the negotiation process, the parties themselves will set the terms of the contract to reflect the relative strength of a patent, the likelihood of a finding of infringement, the potential scope of use of the invention, and a multitude of other factors relevant to their business objectives. Stated simply, if there is any question of the validity of the patent, it can reflect itself in the applicable royalty rate.

The parties should determine the terms of the contract, not this Court. If parties wish to make royalty payments contingent on a patent's validity, they can do so quite easily in the contract itself by specifying that the royalty rate will fall to zero should a court invalidate the patent. Or, as in this case, they can negotiate a license that covers patent appli-

cations as well as issued patents, with both sides recognizing, and contractually allocating, the risks and rewards in such a contract. Here, just that happened—MedImmune obtained advantageous license terms that include a small up-front payment, J.A. 402, a discounted royalty rate, *id.*, a most favored nation clause, *id.* at 405, and a right to terminate the license, in whole or in part, on six month's notice, *id.* at 409. Thus, the actual history of this case shows the truth of the Court's earlier observation that the parties can "resolve[] the uncertainties by their bargain." *Aronson*, 440 U.S. at 264; *cf. D. H. Overmyer Co. v. Frick Co.*, 405 U.S. 174, 187-88 (1972) (enforcing the agreed terms of a contract despite waiver of Fourteenth Amendment due process rights in a cognovit note because the contract was negotiated between sophisticated parties). In short, "it is best to leave contract design to the market, where incentives are aligned rather than ignored. Everyone understands this for the branch of intellectual property that we call trade secrets. It is no less true of . . . patents." Frank H. Easterbrook, *Contract and Copyright*, 42 Hous. L. Rev. 953, 956 (2005).

*Second*, the *Lear* rule discourages people from applying for patents and therefore reduces disclosure of useful inventions. In direct contrast to *Lear*, *Aronson* guarantees certainty in licensing for *unpatented* inventions, even for those contracts negotiated during the pendency of a failed patent applications. "[P]atent-application licensing of this sort is desirable because it encourages patent applications, *promotes early disclosure*, and allows parties to structure their bargains efficiently." *Aronson*, 440 U.S. at 267 (Blackmun, J., concurring in the result) (emphasis added). The same is equally true for licenses dealing with those patent applications that have been approved by the PTO and have become patents.

Indeed, the divergence of *Aronson* and *Lear* leads to bizarre results that reward the unsuccessful patent applicant more than the owner of an issued patent. For example, in

both *Lear* and *Aronson* (and indeed in the case at bar), the parties negotiated the licensing agreements before the patents issued. In *Lear*, this Court refused to enforce the parties' contract because the patent had issued and because the Court was persuaded that "[l]icensees may often be the only individuals with enough economic incentive to challenge the patentability of an inventor's discovery." 395 U.S. at 670. In *Aronson*, however, this Court *enforced* the agreement precisely because the patent application had failed. A rule that gives more rights to the failed patent applicant than to the patent owner would turn patent law on its head. In addition, it directly conflicts with *Aronson*'s analysis of determining preemption based on whether "enforcement of this agreement" would "discourage anyone from seeking a patent." 440 U.S. at 263. Rational inventors considering whether to seek a patent and ultimately disclose their work to the public could well decide that the significant uncertainty in their ability to enforce a patent means that it is better not to apply at all. Instead of disclosing their ideas in a patent application, they would choose to rely solely on trade secret protection and other state laws that offer fewer benefits than a patent but at least allow the inventor to license without fear of judicial intervention.

*Third*, even under the one patent principle identified in *Lear*—"the strong federal policy favoring the full and free use of ideas in the public domain," 395 U.S. at 674—the *Lear* rule is deficient. At the very least, this one goal is not strong enough of its own force to overcome the disincentives that the case imposes on innovation and disclosure. *Lear* permitted licensees to set aside the terms of their agreements under the rationale that "[l]icensees may often be the only individuals with enough economic incentive to challenge the patentability of an inventor's discovery." *Id.* at 670. But this rationale is incorrect on two grounds. First, large competitors of the patent owner also have enormous incentives to challenge a patent, and the patentee often is unwilling to negotiate with

them precisely because it wishes to retain its competitive advantage. Second, it is far from clear why licensees are the only ones capable of challenging a patent. Patents are public, and the ability to discover prior art does not depend in any way, shape, or form on whether the investigator is in a contractual relationship with the patentee. With thousands of potential challengers in a market characterized by more and better information, the older rationale of *Lear* makes no sense today, if it ever did.

Clear licensing rules also facilitate another goal of patent law—the widespread dissemination of information. This objective is a close cousin both to the interest *Lear* identified, a strong federal policy in the free flow of ideas, as well to the fundamental federal interest in disclosure. Dissemination is vital to patent law because it allows the public to have access to the idea. The more a patent is licensed, the more likely it will be used, and the more likely it will spur even further innovation. Certainty promotes increased licensing of patented inventions. The *Lear* rule, by contrast, provides an incentive for patent owners to "hoard" information. *Kewanee*, 416 U.S. at 486. This solution often is sub-optimal for the patent owner and the public because licensing allows for the increased division of labor within the marketplace.

*Lear*'s anti-license bias also adversely affects the public's access to patented ideas in other ways. Many potential licensees are firms seeking to use patented technology to enter new markets or enhance their competitive position in existing ones. Each new licensee may represent a new provider of a patented product. Clarity in licensing increases competition by allowing firms that have little prior experience to work together because they know they can rely on the contract itself to set the terms of the relationship even if the parties have no pre-existing ties. Conversely, a rule that imperils the predictability and enforceability of licensing arrangements would inhibit both cooperation and competition.

Finally, to whatever extent *Lear* was correct in 1969, it has been superseded by developments in Congress. Since 1980, Congress has permitted "[a]ny person at any time" to "file a request for reexamination" of a patent. 35 U.S.C. § 302. A re-examination may be *ex parte* or, since 1999, *inter partes*. *See* 35 U.S.C. §§ 302-307 (*ex parte* reexamination); 311-318 (*inter partes* reexamination). While a reexamination challenge is slightly more limited than a challenge to a patent in an Article III court, its availability nevertheless shows that Congress, not this Court, is in the best position to assess how to encourage challenges to a patent's validity and who should raise them.[2] Because any interpretation of *Lear*, let alone its broadest interpretation, does not further the aims of patent law as expressed by Congress or this Court, it should be overruled or modified to ensure that private parties retain the right to bargain for a patent license in the manner that best fits them.

## II. EVEN IF *LEAR* WERE ALLOWED TO STAND, ITS RATIONALE SHOULD NOT BE EXTENDED AS PROPOSED BY MEDIMMUNE.

*Lear* was incorrect in holding that federal patent policy justified the preemption of state contract law despite ample evidence that the enforcement of license agreements works to achieve, not frustrate, the objectives of the patent system. Regardless of the soundness of the *Lear* rule, however, it does not extend to this case. Here, the licensee does not wish to terminate the agreement but instead wants to retain its own

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[2] Moreover, Congress knows how to legislate in areas regarding the enforceability and propriety of patent licensing agreements. Since *Lear* was decided, Congress also has made clear through the patent misuse statute, 35 U.S.C. § 271(d), that it is not an abuse of the patent for a patent owner to tie different products and services together in a contract so long as the patentee does not have actual market power in the tying patent. *Cf. Illinois Tool Works v. Independent Ink*, 126 S. Ct. 1281, 1290-91 (2006).

benefit of the bargain (the negotiated royalty rate) while depriving the patent holder of the peace it thought it had negotiated through the license. In *Lear*, the Court "s[ought] to balance the claims of promisor and promisee *in accord with the requirements of good faith*." *Lear*, 395 U.S. at 670 (emphasis added). MedImmune's position is inconsistent with the requirements of good faith. Indeed, the types of challenges MedImmune wishes to facilitate do not occur on a regular basis now because of a good-faith belief on the part of both parties that the contract resolves their disputes. At the very least, this Court should not extend *Lear* to enable licensees to challenge patents without terminating their license agreement.

The easiest way to understand *Lear* is to treat it as though it granted the licensee an option to terminate an agreement at any time in order to challenge the validity of the patent. But that option comes with a price because a licensee who wishes to exercise it must abandon the protection furnished by the license and expose itself to serious risks of liability by continuing to use the invention, should the patent turn out to be valid. The unsoundness of the *Lear* rule is therefore mitigated by the reluctance of licensees to challenge their agreements and chance an adverse judgment.

Allowing licensees to avoid this risk would alter settled expectations and call into question the finality of all licenses. Since at least 1997, when the Federal Circuit decided *Studiengesellschaft Kohle, M.B.H. v. Shell Oil Co.*, 112 F.3d 1561 (Fed. Cir. 1997), both parties to a licensing agreement have assumed that a licensee is unable to challenge the licensed patent without first terminating the agreement. Changing such a rule would be a surprise gift to licensees, allowing them to keep the benefit of the agreed royalty rate and enjoy immunity from suit while granting them for no additional consideration the additional, unilateral option to challenge the patent and thereby possibly cancel their ongo-

ing royalty obligations. Moreover, changing the rule could impose on licensors the burden of spending substantial sums in legal fees litigating an issue they thought had been finally resolved. *Cf. American Intellectual Property Law Association Report of the Economic Survey 2003*, at 22 (2003) (noting that the median litigation costs per side in a patent case are $500,000 when less than $1 million is at stake, $2 million when the dispute is between $1-$25 million, and at least $4 million per side when the amount is more than $25 million).

MedImmune's proposed rule also is an open invitation for endless litigation. Patent licenses often represent the settlement of litigation between the patent owner and an alleged infringer. Lemley, *supra*, at 1505 ("[L]itigation may be a useful settlement strategy, forcing the other side to the bargaining table. Indeed, that appears to be what litigation normally is, since the overwhelming majority of patent lawsuits settle, presumably with some form of licensing deal."). Licensing and litigation often go hand-in-hand. *See* John R. Allison et al., *Valuable Patents*, 92 Geo. L. J. 435, 439-40 (2004).

Under petitioner's proposed rule, however, the parties could never finally resolve a case because the licensee would retain the unwaivable right to challenge the license negotiated as part of the settlement agreement. Suppose, for example, that a defendant in a patent infringement lawsuit settles on the eve of trial by taking a license that calls for payment of an amount discounted from the damages the plaintiff sought at trial. Should that same defendant now be able to bring a declaratory judgment action challenging the validity of the patent, having locked in the royalty rate at the settlement price? A rule permitting such behavior would undermine business stability, discourage settlement, and decrease the incentives to file for a patent in the first instance, solely by

raising the cost to patent holders of obtaining monetary rewards for their inventions.

Indeed, the incongruity of letting a licensee set aside a license negotiated as part of a settlement agreement shows why declaratory judgment actions are manifestly inappropriate whenever a license exists. The entire purpose of a settlement agreement is to bring cases to closure, which any subsequent litigation undoes. A contrary rule would force a patent owner to litigate through final judgment and appeal or face the risk that licensees will reignite the lawsuit at a time of their own choosing. A declaratory judgment action stemming from a license negotiated as part of a settlement makes no sense precisely because the settlement itself resolves the "controversy." *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240 (1937).

The rule is no more sensible in the context of license agreements negotiated without the filing of a suit: Taking a license resolves the controversy. Both pre-suit and post-suit, the patent holder has only one enforcement mechanism—a lawsuit to enforce the right to exclude under 35 U.S.C. § 281. That statute, entitled "Remedy for infringement of patent," states in full: "A patentee shall have remedy by civil action for infringement of his patent." A patent is not self-enforcing. It only grants the owner the right to bring a lawsuit and prove infringement of a valid and enforceable patent. A court awards injunctive relief, 35 U.S.C. § 283, damages, 35 U.S.C. § 284, or attorney fees, 35 U.S.C. § 285, only if a patent owner prevails in litigation. Whether the patent holder actually has filed suit often turns on the degree of success achieved in pre-suit negotiations. Yet treating licenses negotiated as part of a settlement in a different manner from licenses negotiated pre-suit would simply encourage patent holders to file a lawsuit before beginning any serious licensing discussions.

The most dramatic increase in litigation produced by MedImmune's rule, however, will come from licensees who will begin bringing declaratory judgment actions. If licensees can retain their licenses while challenging patents at the same time, it is a no-risk proposition for them but a source of substantial unfairness to licensors. For the licensee, bringing a lawsuit might well make economic sense whenever the litigation costs are less than the royalty obligation to the patent holder. Even by simply confronting the licensor with the burdens of litigation, a licensee may be able to induce a renegotiation of royalties, regardless of the merit of the licensee's invalidity contentions. These added costs will place a heavy burden on the holders of valid patents while giving licensees a free shot at challenging a patent. Under such circumstances, an overwhelming increase in litigation is predictable.

Ultimately, the proposed rule will adversely affect not just licensors, but many licensees as well. All licensees will pay more as patent owners increase the cost of a license—particularly through higher up-front payments—in order to factor in the additional inconvenience, expense, and risk of enhanced litigation exposure. Such a rule will particularly disadvantage those licensees who are quite content to respect the patent terms in full. They, too, will face enhanced royalty costs because they cannot offer any binding legal assurance to the licensor of their willingness to adhere to the negotiated agreement. *Cf.* Schlicher, *A Lear v. Adkins Allegory*, 68 J. Pat. & Trademark Off. Soc'y at 433; Br. of United States as *Amicus Curiae*, *Aronson v. Quick Point Pencil*, at 23 n. 11. MedImmune's proposed rule will benefit only those licensees who, *ex post*, want to escape from the terms of their contract.

* * * * *

If this Court holds that neither Article III nor the Declaratory Judgment Act prohibits these types of challenges, it is even more important that the Court also make clear that

*Lear* does not pose an obstacle for parties who want to bargain for certainty in licensing agreements. *Cf.* Brief of *Amicus Curiae* Licensing Executives Society in Support of Neither Party (arguing that the Court should use this opportunity to clarify the scope of *Lear*). The Court should allow private parties to negotiate clauses such as "no-contest" provisions that would prevent a licensee from challenging the patent, or other clauses that would help achieve finality in the resolution of disputes. At the very least, the Court should not go beyond *Lear*, and should require licensees to terminate their licenses before bringing suit. Sophisticated parties should be able to make such agreements without fear that their contract will be preempted.

As licensing specialists we see no reason to further undermine the operation of the patent system by making it easier for parties to abrogate contracts that reflected their joint intention when formed. It seems almost grotesque to hold that federal patent law preempts the very features of state contract law that help enhance the value of the patent system. Regardless of whether this Court decides to modify the *Lear* rule itself, it should reject MedImmune's attempt to produce an unwarranted extension of that unsound principle. The Court should avoid the serious dislocation to the patent system that will surely follow from such a result.

## CONCLUSION

The judgment of the court of appeals should be affirmed.

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IN THE
# Supreme Court of the United States

## MEDIMMUNE, INC.,
*Petitioner,*

v.

## GENENTECH, INC. AND CITY OF HOPE NATIONAL MEDICAL CENTER,
*Respondents.*

**On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit**

## BRIEF OF THREE INTELLECTUAL PROPERTY PROFESSORS AS *AMICI CURIAE* IN SUPPORT OF THE PETITIONER

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## CONSENTS TO FILE AND INTEREST OF THE *AMICI CURIAE*

Through their counsel of record, all parties to this appeal have consented in writing to the filing of this brief. Copies of the consents accompanied this brief.

The individuals Jay Dratler, Jr., Jeffrey M. Samuels, and A. Samuel Oddi (collectively, "Amici") are all attorneys and chaired professors of law. Two (Jay Dratler, Jr. and A. Samuel Oddi) are admitted to practice before this Court.

The interest of Amici in this case arises from lifetimes of study, research and practice in the field of intellectual property law. Jay Dratler, Jr. has thought and written about declaratory judgments in patent cases for twelve years, since his two-volume loose-leaf treatise on licensing was first published in 1994. See 1 Jay Dratler, Jr., *Licensing of Intellectual Property* § 2.01[1][a][iii] (Law Journal Press 1994 & Supps.) Jeffrey M. Samuels was Assistant Commissioner of Patents and Trademarks from November 1987 to January 1993. A. Samuel Oddi served as patent counsel for major corporations for over ten years and has taught law for over 30 years. Although we are not submitting the Brief on behalf of any organization, we all work at the Intellectual Property and Technology Center at the University of Akron School of Law, which is dedicated to the advancement of law and policy in the field of intellectual property.[1]

[1] The University of Akron has provided office services and will reimburse out-of-pocket expenses related to this brief. This brief, however, is not submitted on behalf of the University of Akron, which has not reviewed and does not endorse its content.

From time to time each of us acts as a paid attorney or consultant. To our knowledge, however, no current or likely future client of any of us has any pecuniary interest in the outcome of this lawsuit. We thus occupy a unique position of expertise and financial disinterest. Our interest is in a patent system that is legally sound and economically rational.

## SUMMARY OF ARGUMENT

In a consistent line of cases extending over six decades, this Court has emphasized the importance of tearing down barriers to challenging patents' validity, lest the public be harmed by unjustified monopolies. Yet the Federal Circuit has categorically refused to allow patent licensees in good standing to challenge the validity or enforceability of the patents they have licensed, although licensees are often the ones best motivated to make such challenges. The Federal Circuit has thus ignored this Court's clear directives and undermined this Court's holding in *Lear, Inc. v. Adkins*.

The source of the problem is the Federal Circuit's "reasonable apprehension of suit" test for declaratory-judgment jurisdiction. That test grants "quiescent" patentees—those who do not threaten suit or charge infringement—effective immunity from challenges to their patents by way of declaratory judgment. They can notify the industry of their patents, enter licensing negotiations, grant licenses, or walk away from the table, all without losing this "immunity" from suit. The Federal Circuit has thus given patentees clear instructions for nullifying the Declaratory Judgment Act in the field of patent law.

The Federal Circuit has held that the Constitution's requirement for a case or controversy dictates this result. That is simply not so. The case or controversy requirement is a limitation on constitutional government, based on the separation of powers. It prevents the judiciary from invading the domain of the legislative or executive branch by deciding abstract or hypothetical questions not raised in a real, concrete dispute between adverse parties. Instead, the Federal Circuit appears to have interpreted it as a rule of litigation fairness or procedural priority, under which a quiescent patentee should not be sued first. That interpretation expands the case or controversy requirement well beyond its rationale.

There may be patent cases in which actions for declaratory judgments are not justiciable, but this case is not one of them. Real issues of justiciability may arise if a party concerned about potential liability for patent infringement requests a declaratory judgment challenging the patent before producing any product on which the patent's claims might be read. In that case a judgment on the patent's validity could be viewed as hypothetical or advisory.

No such difficulty arises in this case. Here Appellant is producing a real product, and there is a real and concrete dispute over whether royalties are due on it. No fact or evidence needed to determine whether the patent is valid and enforceable depends upon whether the license is in force or has been breached or terminated. There is therefore nothing hypothetical or abstract about this case.

Nor would adjudication provide a mere advisory opinion. On the contrary, it would clarify alleged legal rights that directly affect the economic interests of the

patentee, the licensee, the industry and the public. Because this case involves medical products, its outcome may affect the public health as well.

Patent law needs a new standard for the justiciability of declaratory-judgment actions—one consistent with the Declaratory Judgment Act and with the real purposes of Article III's case or controversy requirement. The Federal Circuit's test is not only inconsistent with this Court's decisions and the Act. It is also economically harmful, for it keeps courts from reviewing "bad" patents even as they are on the rise.

At a minimum, a new standard should treat patentees and their adversaries symmetrically. A licensee should be able to request a declaratory judgment whenever a patentee could sue for infringement if the license did not exist, as long as there is a real, current dispute between the parties that the court's judgment can resolve.

Modern standing doctrine's requirement for "injury in fact" does not stand in the way. It does so only if interpreted literally, as requiring invasion of a protected interest. But in patent cases such an interpretation is circular: even a confessed infringer does not invade the patentee's rights unless the patent is valid—a decision that only the court can make. A literal interpretation of injury in fact would eliminate declaratory judgments from all of patent law.

A patent's validity or enforceability is almost always uncertain. The uncertainty impacts both patentees and their adversaries. It has direct and often enormous economic consequences and is the source of very real disputes. Therefore, in patent cases, "injury in fact" exists whenever

doubt about a patent's validity or enforceability is real enough to engender non-pretextual disputes that a court can resolve.

The uncertainty itself—not either party—causes the economic injury. The Declaratory Judgment Act provides a means to resolve the uncertainty, and thereby to prevent or redress the injury, when the alleged rightholder declines to sue. Any justiciability doctrine that fails to recognize these economic facts of life will not only nullify the Declaratory Judgment Act in the field of patents; it will also contravene decades of precedent. Surely nothing in Article III, which seeks only to keeps courts from performing legislative or executive functions, requires such an extreme result.

## ARGUMENT

### I. The result and reasoning below contravene consistent directives of this Court to respect the importance of testing patents in court.

In a long line of cases stretching back at least six decades, this Court has repeatedly ruled that testing patents for validity and enforceability has paramount importance in the scheme of patent law. *See Cardinal Chemical Co. v. Morton International, Inc.*, 508 U.S. 83, 100-101 (1993) (pointing out "the wasteful consequences of relitigating the validity of a patent after it has once been held invalid in a fair trial" and "the danger that the opportunity to relitigate might, as a practical matter, grant monopoly privileges to the holders of invalid patents") (footnotes omitted); *Blonder Tongue Laboratories, Inc. v. University of Illinois Foundation*, 402 U.S. 313, 344 (1971); *Lear, Inc. v. Adkins*,

395 U.S. 653, 670-671 (1969); *Precision Instrument Manufacturing Co. v. Automotive Maintenance Machinery Co.*, 324 U.S. 806, 816 (1945) (noting public's "paramount interest in seeing that patent monopolies spring from backgrounds free from fraud or other inequitable conduct and that such monopolies are kept within their legitimate scope").

The linchpin of these cases is this Court's decision in *Blonder Tongue*, 402 U.S. at 350, abandoning the doctrine of mutuality of estoppel in patent cases. It ruled that a final judgment of patent invalidity, if based on a full and fair trial, estops the patentee from asserting the same patent against *anyone*. *See id.*, 402 U.S. at 328-329.

Under *Blonder Tongue*, a patent is dead once declared invalid in a single lawsuit. It can no longer threaten industry, curtail free competition, or harm the public. In announcing this rule, this Court relied heavily on the great expense and delay of patent litigation and the general public's strong economic interest in insuring that invalid patents do not create unjustified economic monopolies. *See id.*, 402 U.S. at 334, 337 & n.31 (noting expense and delay); 402 U.S. at 346 (noting competitive impact).

Twenty-two years later, in *Cardinal Chemical*, this Court applied the same principles to curtail an odd procedural practice that the Federal Circuit had developed. That court had routinely vacated trial-court judgments of patent invalidity after upholding findings that the patent was not infringed. *See Cardinal Chemical*, *supra*, 508 U.S. at 85, 89-90, 95.

Bare logic supported the procedure: if a patent is not infringed, it does not matter *for that case* whether or not it is valid. But this Court repudiated the Federal Circuit's formalistic logic. *See id.*, 508 U.S. at 102. It reasoned that the accused infringer had paid dearly in time and money for the judgment of invalidity, and that both industry and the public had a strong interest in that judgment under *Blonder-Tongue*. *See id.*, 508 U.S. at 99 (noting interest of litigant); 508 U.S. at 100 (noting "importance to the public at large of resolving questions of patent validity"); *id.*, 508 U.S. at 102 (both).

The case of *Lear, Inc. v. Adkins* is much closer to this case. There this Court addressed whether a patent licensee could challenge the validity of the licensed patent. The specific issue was the continuing validity of the doctrine of licensee estoppel, under which a licensee, by virtue of taking a license, was deemed to have recognized the validity of the licensed patent and to be estopped from challenging it. *See Lear*, *supra*, 395 U.S. at 656. Characterizing that principle as a matter of contract under state law, this Court held it superseded by fundamental patent principles. *See id.*, 395 U.S. at 670-671. This Court referred generally to the need to encourage legal challenges to invalid patents and specifically to the benefits of encouraging those with the greatest economic incentives to make challenges to do so. "Licensees," it said, "may often be the only individuals with enough economic incentive to challenge the patentability of an inventor's discovery. If they are muzzled, the public may continually be required to pay tribute to would-be monopolists without need or justification." *Id.*, 395 U.S. at 670.

Together, these cases provide a consistent and formidable body of precedent establishing three principles. First, patent law protects our economy, future innovation and the public from unjustified patent monopolies by encouraging invalid or unenforceable patents to be challenged and declared as such. Second, the law disfavors any procedural mechanism that hinders or delays such challenges or declarations. Third, patent law encourages challenges to patents by "private attorneys general" motivated by their own economic self-interest to protect the public interest, and the class of private attorneys general includes patent licensees.

The result and rationale below contravene these principles. By precluding all patent licensees in good standing from challenging the validity or enforceability of their licensed patents, it eliminates a large and important class of potential patent challenges. By requiring licensees to repudiate, breach or terminate their license agreements before mounting challenges by way of declaratory judgment, it hinders and delays those challenges. It thus discourages challenges to patents by those most highly motivated to make them.

## II. The Federal Circuit's "reasonable apprehension of suit" test, formalistically applied by that court, virtually nullifies the Declaratory Judgment Act in the field of patent law.

The touchstone of the Federal Circuit's analysis in this case is its "reasonable apprehension of suit" test for federal declaratory judgment jurisdiction. *See*, e.g., *BP Chemicals, Ltd. v. Union Carbide Corp.*, 4 F.3d 975, 978 (Fed. Cir. 1993); *Shell Oil Co. v. Amoco Corp.*, 970 F.2d 885, 887-

888 n.2 (Fed. Cir. 1992); *Spectronics Corp. v. H.B. Fuller Co.*, 940 F.2d 631, 634 (Fed. Cir.), *cert. denied*, 502 U.S. 1013 (1991).[2] No such jurisdiction exists in this case, that court held, because the license agreement precluded any reasonable apprehension that the patentee would sue. *See MedImmune, Inc. v. Genentech, Inc.*, 427 F.3d 958, 962-965 (Fed. Cir. 2005).

This Court has never reviewed the Federal Circuit's "reasonable apprehension of suit" test. As the Federal Circuit has repeatedly stressed, it is an objective test, which depends upon the patentee's actions. *See*, e.g., *BP Chemicals*, 4 F.3d at 980; *Arrowhead Industrial Water, Inc. v. Ecolochem, Inc.*, 846 F.2d 731, 736 (Fed. Cir. 1988); *International Medical Prosthetics Research Associates, Inc. v. Gore Enterprise Holdings, Inc.*, 787 F.2d 572, 575 (Fed. Cir. 1986).

The test allows a patentee to avoid a suit for declaratory judgment if it is "quiescent," i.e., if it makes no threat of suit or charge of infringement. *See Arrowhead Industrial Water*, 846 F.2d at 736 (if "defendant has done nothing but obtain a patent, there can be no basis for the required apprehension, a rule that protects quiescent patent owners against unwarranted litigation") (citations omitted). But this does not mean that the patentee must refrain from

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[2] The test actually has two prongs: (1) the declaratory plaintiff's reasonable apprehension of suit by the patentee and (2) the declaratory plaintiff's engagement in or preparation for infringing activity. See *BP Chemicals*, 4 F.3d at 978; *Spectronics Corp.*, 940 F.2d at 634. The second or "infringement" prong, however, is not at issue in this appeal. Respondent Genentech's assertion that its licensed patent covered Appellant's production and sale of the product Synagis® is tantamount to an assertion that those activities would infringe the patent in the absence of a license.

affecting an industry or the economy. The patentee can circulate its patent to competitors and the industry. *See Spectronics*, 940 F.2d at 632-633, 636-638 (patentee's letters to industry announcing addition of patent to its "growing family of patents" and its patent strategy, without referring to any competing products, did not create basis for declaratory judgment action). The patentee can discuss licensing. *See Shell Oil*, 970 F.2d at 889 (there was no reasonable apprehension of suit where patentee responded to plaintiff's initiatives and entered licensing negotiations, during course of which it referred to plaintiff's catalyst as "falling within" or "covered under" patent and said it would enforce patent). The patentee can even refuse a license and break off negotiations. *See*, e.g., *Teva Pharmaceuticals USA, Inc. v. Pfizer Inc.*, 395 F.3d 1324, 1327, 1329-1330 (Fed. Cir. 2005) (court had no declaratory judgment jurisdiction although patentee had listed patent in FDA's "Orange Book" and had sued and later licensed other generic maker, where it had refused to license declaratory plaintiff on request or to sue it for infringement); *Cygnus Therapeutic Systems v. ALZA Corp.*, 92 F.3d 1153, 1156-1157, 1159-1160 (Fed. Cir. 1996), *overruled on other ground*, *Nobelpharma AB v. Implant Innovations, Inc.*, 141 F.3d 1059, 1068 & n.5 (Fed. Cir. 1998) (*en banc* on that other ground only) (there was no reasonable apprehension of suit where patentee's officers (1) stated that declaratory plaintiff's continuing its research program "made no sense" due to existence of patent; (2) reported that patent had survived reexamination; and (3) insisted that patentee had "a very strong proprietary position[,]" and where patentee refused to license declaratory plaintiff; patentee had done nothing more than exercise its right to exclude).

In practice, these results give patentees a practical prescription for nullifying the Declaratory Judgment Act in the field of patent law. All they have to do is stay "quiescent" by refraining from threats of suit or charges of infringement. In the meantime, they can make an entire industry aware of their patent, conclude licensing agreements, collect royalties, and scare off unlicensed competition by the fear of patent litigation. Any unlicensed competitor that invests in plant and production without a license will risk a total loss of sunk investment if the patentee sues for infringement after production begins, wins the suit, and gets an injunction, which is now a standard remedy.[3]

A moment's thought reveals how this test frustrates the Declaratory Judgment Act's purpose. The Act allows courts to "declare the rights and other legal relations of any interested party seeking such declaration[.]" 28 U.S.C. § 2201(a) (in part). It thus lets a plaintiff clarify uncertain rights and legal relations when the other party to the dispute declines to do so. *See Travelers Insurance Co. v. Davis*, 490 F.2d 536, 543 (3d Cir. 1974). Yet by requiring the plaintiff to have a "reasonable apprehension of suit" based upon the defendant's objective manifestations, the Federal

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[3] The question whether injunctive relief will *remain* a standard remedy in a successful patent infringement suit is now before this Court in a separate case. *See eBay Inc. v. MercExchange, LLC*, 126 S.Ct. 733, 74 U.S.L.W. 3321 (2005) (granting *certiorari* to decide issue). The law that this Court will review, however, is now to that effect. *See MercExchange, LLC v. eBay, Inc.*, 401 F.3d 1323, 1338 (Fed. Cir. 2005), *cert. granted, supra* ("Because the 'right to exclude recognized in a patent is but the essence of the concept of property,' the general rule is that a permanent injunction will issue once infringement and validity have been adjudged"), quoting *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1246-1247 (Fed. Cir. 1989).

Circuit allows the defendant to control the existence and timing of litigation. That is precisely the result that the Declaratory Judgment Act sought to avoid. Without clear guidance and instructions from this Court, the Federal Circuit will continue to allow patentees to nullify the Declaratory Judgment Act in this manner.

## III. Nothing in the Constitution's case or controversy requirement mandates the Federal Circuit's test.

Last year two judges of a three-judge panel decided that the Constitution's case or controversy requirement mandates the "reasonable apprehension of suit" test. *See Teva Pharmaceuticals*, 395 F.3d at 1335 (Fed. Cir. 2005). There was a strong dissent. *See id.*, 395 F.3d at 1339 (Chief Judge Mayer, dissenting). Yet this was not the first time the Federal Circuit has flirted with constitutionalizing its test. *See Foster v. Hallco Manufacturing Co.*, 947 F.2d 469, 479 (Fed. Cir. 1991) (in patent context, "case or controversy" requirement demands "sufficient acts by both parties which support an actual charge of infringement or at least a reasonable belief that a suit for infringement will be brought") (citation omitted).

To the extent one can read a rationale in the Federal Circuit's decisions, it appears to be a matter of fairness and litigation priority. The *Teva Pharmaceuticals* panel seemed to feel that it would be unfair and inappropriate for "quiescent" patentees to suffer suit or to lose their choice of the forum and timing for suit. *See Teva Pharmaceuticals*, 395 F.3d at 1334 (majority opinion) (patentee "need not" sue declaratory plaintiff "immediately" because third party's 180-day exclusivity period under Hatch-Waxman Act would prevent declaratory plaintiff from marketing

putatively infringing generic drug until six months after relevant patent expired). A direct precedent for the Federal Circuit's decision in the case at bar suggested a similar rationale:

> [P]ermitting [the patent licensee] to pursue a lawsuit without materially breaching its license agreement yields undesirable results. [The licensor] voluntarily relinquished its statutory right to exclude by granting [the licensee] a nonexclusive license. In so doing, [the licensor] chose to avoid litigation as an avenue of enforcing its rights. Allowing this action to proceed would effectively defeat those contractual covenants and discourage patentees from granting licenses. In other words, in this situation, the licensor would bear all the risk, while licensee would benefit from the license's effective cap on damages or royalties in the event its challenge to the patent's scope or validity fails.

*Gen-Probe, Inc. v. Vysis, Inc.*, 359 F.3d 1376, 1382 (Fed. Cir. 2004).

But the Constitution's case or controversy requirement has nothing to do with litigation fairness, priority of suit, or the choice of forum or timing of litigation. It is a matter of constitutional governance and the separation of powers. *See, e.g., Flast v. Cohen*, 392 U.S. 83, 96 (1968) ("Federal judicial power is limited to those disputes which confine federal courts to a role consistent with a system of separated powers and which are traditionally thought to be capable of resolution through the judicial process"); *Valley Forge Christian College v. Americans United for Separation of Church and State*, 454 U.S. 464, 473 1982). The case or controversy requirement insures that courts will

decide nothing except against the background of specific facts in a specific dispute among real and adverse parties. *See Aetna Life Insurance Co. v. Haworth*, 300 U.S. 227, 240 (1937). In so doing, it keeps courts out of the legislature's and executive's domains, where decisions can be made based on general policy, speculation, and prediction.

Therefore the touchstone of the case or controversy requirement is the distinction between a dispositive decision in a concrete case between adverse parties based on real facts and an advisory opinion based on hypothetical facts or speculation. *See Aetna*, 300 U.S. at 240-241. The former is the function of the judiciary, the latter of Congress and the executive branch.

On its face, a reasonable apprehension of suit has little to do with this distinction. The Declaratory Judgment Act's animating principle is that real parties may have real, present and concrete adverse interests in a determination of rights or legal relations that a court can grant specifically and conclusively in a dispositive opinion, but that one party may wish to postpone or avoid for reasons of its own. If all relevant facts are known and in evidence, the Act gives the party desiring resolution the right to have it despite the other party's wish for delay. There is nothing necessarily hypothetical, abstract, or "legislative" about such a resolution, and nothing in one party's attempts to avoid a resolution—for example, by refraining from threats and charges—makes it so.

## IV. There may be requests for declaratory judgments in patent cases that are not cases or controversies in a constitutional sense, but the case at bar is not one of them.

Petitioner here asked the district court to declare that the licensed patent is invalid or unenforceable. Both issues are real, concrete and ripe for adjudication.

Under the Federal Circuit's own precedent, a patent's validity is almost entirely a documentary issue. In order to assess its validity, the court must first construe the patent's claims. *See Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996) (courts, not juries, construe patent claims). The Federal Circuit, however, has limited the evidence to be used for this purpose to the public record, including the patent and its prosecution history. *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). By statutory command, evidence of the invention's obviousness or lack of novelty—so-called "prior art"—must have existed at the time the invention was made or, at the latest, before the patent application was filed. *See* 35 U.S.C. §§ 102, 103(a). Therefore the facts and evidence necessary to decide a patent's validity—the patent itself, its prosecution history, prior art cited in the patent, other prior art, and relevant technical references—are all available when the patent issues. The purely legal question of a patent's validity is therefore almost *never* hypothetical or abstract.

What might make a request for a *judgment* of patent invalidity hypothetical or abstract in the sense of Article III is the position of the party asking for a judgment. If a plaintiff seeks a declaratory judgment before ever producing a product on which the patent claims might be

read, then no case or controversy may exist because the plaintiff's interest is simply too abstract and hypothetical. *Cf. Lang v. Pacific Marine and Supply Co.*, 895 F.2d 761, 763, 764-765 (Fed. Cir. 1990) (affirming dismissal of claim by patentee for declaratory judgment that ship would infringe dominant patent where ship would not be finished for nine months after complaint was filed).

But that is not this case. Here Appellant is currently producing a product called Synagis® on which the patentee claims royalties under the license. There is therefore a product on which the patent's claims can be read. All the evidence needed to produce a final, concrete decision on both validity and infringement exists now. The only thing standing in the way of a trial, in the Federal Circuit's view, is the license agreement and therefore the absence of a reasonable apprehension that the patentee will sue. But nothing bearing on the patent's validity or enforceability turns on whether the license is in effect or has been breached or terminated.

If the patentee had chosen to sue before granting a license, the dispute would have presented a classic patent infringement case—as clear a case or controversy as exists in patent law. Surely whether a case or controversy exists under Article III cannot turn solely on who sues first. If it did, the Declaratory Judgment Act would be a dead letter in all fields, not just patent law.

Like validity, the issue of enforceability is largely documentary. Unenforceability for inequitable conduct—a patent applicant's culpable failure to disclose known and material prior art to the patent examiner—depends on prior art and acts of nondisclosure before the patent issues. *See* 1 Jay Dratler, Jr., *Intellectual Property Law: Commercial,*

*Creative, and Industrial Property* § 2.08[2] (Law Journal Press 1991 & Supps.). Another cause of unenforceability, patent misuse, may turn on conduct occurring after the patent issues, but that conduct must have occurred before the case is filed. *See* 1 Jay Dratler, Jr., *Licensing of Intellectual Property* § 5.04 (Law Journal Press 1994 & Supps.) (hereinafter, "Dratler Licensing"). Here again, the existence of a case or controversy depends mostly on how close to producing a putatively infringing product the declaratory plaintiff was at the time of suit. The existence *vel non* of a license agreement is irrelevant, except to the extent that the license itself may be evidence of misuse.

## V. Patent law needs a new standard for declaratory judgment, one consistent with the Declaratory Judgment Act and the purpose of the Constitution's case or controversy requirement.

### A. The Federal Circuit's "reasonable apprehension of suit" test is bad economics as well as bad law.

The Federal Circuit's test ignores this Court's repeated instructions to construe patent law so as to permit and encourage legal challenges to possibly invalid patents by private attorneys general whose real and concrete economic interests insure a case or controversy and a legitimate reason for the challenge. *See supra* Part I.

Today those instructions are more important then ever before. Evidence is mounting that an increasing number of "bad" patents are issuing on "inventions" that do not quality for legal monopolies. Some commentators believe the problem derives from poor incentives and lack of resources within the Patent and Trademark Office (PTO).

*See* Adam B. Jaffe and Josh Lerner, *Innovation and Its Discontents: How Our Broken Patent System is Endangering Innovation and Progress, and What to Do About It* 34 (Princeton University Press 2004) ("As a result of legal and administrative changes made between 1982 and 1990, the PTO has become so overtaxed, and its incentives have become so skewed toward granting patents, that the tests for novelty and non-obviousness that are supposed to insure that the patent monopoly is granted only to true inventors have become largely non-operative"). Some criticize the Federal Circuit's failure to prescribe reasonable limits on the scope of patentable subject matter. *See, e.g.*, Jay Dratler, Jr., "Alice in Wonderland Meets the U.S. Patent System," 38 Akron L. Rev. 299, 308-319 (2005) (hereinafter "Alice"); John R. Thomas, "The Patenting of the Liberal Professions," 40 B.C. L. Rev. 1139, 1163-1164 (1999).[4] Some see a failure of the PTO and the courts to recognize the dividing line between legitimate patents on inventions and prohibited monopolies on businesses in our free-market economy. *See* "To

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[4] Professor Thomas has suggested that the Federal Circuit's refusal to restrain the expansion of patentable subject matter may ultimately produce patents on the work product of lawyers and priests:

> With business and medical techniques firmly under wing, and patents on sports methods and procedures of psychological analysis trickling out of the Patent Office, patents appropriating almost any sort of communicable practice seem easily attainable. . . . Under increasingly permissive Federal Circuit case law, techniques within such far-flung disciplines as language, the fine arts and theology also now appear to be within the realm of patentability.

40 B.C. L. Rev. at 1163-1164.

Promote Innovation: the Proper Balance of Competition and Patent Law and Policy, A Report by the Federal Trade Commission," Executive Summary at 5 (Oct. 2003) ("FTC Innovation Report") ("[M]any participants in and observers of the patent system expressed significant concerns that, in some ways, the patent system is out of balance with competition policy"). *See also*, Jay Dratler, Jr., "Does Lord Darcy Yet Live? The Case Against Software and Business-Method Patents," 43 Santa Clara L. Rev. 823 (2003) (arguing that Federal Circuit's receptivity to patents on computer programs and business methods shifts line between competition and invention in place under Anglo-American law since 1623 by granting monopolies on what are essentially ideas for businesses devoid of technological risk). Some see a failure to impose consistent and discerning standards of nonobviousness. *See* FTC Innovation Report, Executive Summary at 10-11 (recommending that nonobviousness standard be tightened); Alice, 38 Akron L. Rev. at 309-319 (arguing that current standard of nonobviousness departs from the spirit of Thomas Jefferson's original standard by emphasizing cognitive difficulty over economic factors like risk).

Yet whatever the reason, the chorus of discontent is growing. For the first time in recent memory, representatives of industry itself are beginning to question whether some aspects of our patent system might impede, rather than promote, technological innovation. *See* FTC Innovation Report, Ch. 3 at 34-37 (discussing how patent "thickets" impede innovation in the electronics industry and noting 90,000 patents held by 10,000 parties relating to microprocessors alone); *id.*, Ch. 3 at 50-55 (similar conclusions for software and Internet industries).

One reform bill now before Congress implicitly recognizes that something is awry. *See* 2005 H.R. 2795 (Smith). It proposes a system of post-grant review of issued patents, like those in many foreign countries, subject to full judicial review. *See id.*, § 9 (proposing new Chapter 32 of Title 35 for post-grant review). If adopted, that system would supplement already existing options for *ex parte* reexamination, *see* 35 U.S.C. ch. 30, §§ 301-307, and *inter partes* reexamination, *see* 35 U.S.C. ch. 31, §§ 311-318. The very existence of a proposal for yet a third means of reviewing already-issued patents suggests the need for some sort of substantive reform.

Given the Federal Circuit's exclusive jurisdiction over patent appeals, *see* 28 U.S.C. § 1295(a)(1), (4)(A), (4)(C), plus the legal and technological complexity of patent cases, this Court has understandably been reluctant to micromanage the Federal Circuit's substantive judgments in the area of its special expertise. *See Warner-Jenkinson Co. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 40 (1997). But this Court has never shrunk from insuring that *all* courts, including patent courts, observe proper procedure and proper procedural standards. *See, e.g., Holmes Group, Inc. v. Vornado Air Circulation Systems, Inc.*, 535 U.S. 826, 830, 833-834 (2005) (reinforcing well-pleaded complaint rule for subject matter jurisdiction and vacating Federal Circuit's decision); *Cardinal Chemical Co.*, 508 U.S. at 100-101 (repudiating Federal Circuit's practice of vacating holdings of patent invalidity after affirming holdings of noninfringement); *Christianson v. Colt Industries Operating Corp.*, 486 U.S. 800, 811, 819 (1988) (reinforcing "well-pleaded complaint" rule for subject-matter jurisdiction and overturning Federal Circuit's reluctant acceptance of jurisdiction after jurisdictional "ping-pong match" with Seventh Circuit); *Blonder Tongue*,

402 U.S. at 344 (abolishing doctrine of mutuality of estoppel in patent cases, discussed in Part I *supra*); *Lear*, 395 U.S. at 670-671 (abolishing doctrine of licensee estoppel in patent cases).

From an economic perspective, this case involves one of the most important procedural issues that this Court may ever resolve. Many patent licensees agree to take licenses and to pay royalties not because they think the patents they license are good ones, but because the economic risks of being wrong are too great. *See* Dratler Licensing, § 2.02[1][a][ii], [iii][C], [iv]. If they forego a license, proceed with a potentially infringing business, and wait to be sued for infringement, they take two immense risks. First, they risk damage liability for up to six years' worth of potentially infringing production. *See* 35 U.S.C. § 286. Second, if they lose an infringement suit, they risk a shut-down injunction[5] that would devalue their entire sunk investment in research, development, planning, plant, production, distribution and marketing. *See* Dratler Licensing, § 2.02[1][a][ii].

Licensees might have thought that Congress resolved this dilemma when it adopted the Declaratory Judgment Act. Yet the Federal Circuit's "reasonable apprehension of suit" test prevents them from bringing declaratory actions to challenge licensed patents while the licenses are in force. It thus throws them right back on the horns of their old dilemma. *See id.*, § 2.02[1][a][iv].

The dilemma gains importance today, when "bad" patents are on the rise. The more uncertain patents there are, the greater their uncertainty, and the greater the

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[5] See note 3 *supra*.

economic importance of industries they cover, the greater the risk of loss to a business that refuses to take a license. As the incentive to sign a license increases, the chance that anyone will challenge shaky patents decreases. The law thus encourages owners of shaky patents to transform their very uncertainty—the "friction" in our legal system—into gold. Their gain, achieved without testing their patents in court, comes at the expense of their competitive rivals, industry, innovation, and the public.

### B. A proper standard for a declaratory-judgment suit by a patent licensee would permit suit whenever the licensee has a real, concrete and non-pretextual reason for seeking release from the license's obligations and the patentee would have a justiciable action for infringement in the absence of the license.

The Declaratory Judgment Act is "only" procedural; it does not, and cannot, expand the reach of judicial power beyond the limits imposed by Article III. *See Aetna*, 300 U.S. at 240. Yet the Act seeks to exploit the full reach of judicial power. *See id.*, 300 U.S. at 239-240 (reference to "actual controversy" in Act "manifestly has regard to the constitutional provision and is operative only in respect to controversies which are such in the constitutional sense"); *id.*, 300 U.S. at 240 ("The word 'actual' [in the Act] is one of emphasis rather than of definition").

A proper test for declaratory-judgment jurisdiction therefore would recognize the Act's intention to authorize declaratory actions up to the constitutional limits. Indeed, it would begin and end with those limits.

Under modern standing doctrine, the constitutional limits involve four distinct analytical elements. The first is the concreteness required of requests for declaratory judgments, i.e., a real, concrete dispute, as distinguished from an abstract or hypothetical case or request for an advisory opinion. *See Aetna*, 300 U.S. at 241 (dispute "must be a real and substantial controversy admitting of specific relief through a decree of a conclusive character, as distinguished from an opinion advising what the law would be upon a hypothetical state of facts") (citation omitted). *See also, Maryland Casualty Co. v. Pacific Coal & Oil Co.*, 312 U.S. 270, 273 (1941). The second element is the "resolvability" required both for declaratory judgments, *see Aetna*, 300 U.S. at 241, and for general constitutional standing, *see Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560 (1992). The dispute must be one that a court can resolve finally by granting the requested judgment. The third and fourth elements are injury in fact and causation thereof, which the modern doctrine of constitutional standing requires. There must be "an invasion of a legally protected interest" and "a causal connection between the injury and the conduct complained of . . . ." *Lujan*, 505 U.S. at 560 (citations omitted).

In the present context, "concreteness" exists whenever, in the absence of the license, the patentee's infringement claim would be justiciable and the licensee has an economic interest in the adjudication that is real, non-pretextual and concrete. In that case the licensee's production or preparation for production provides something on which to read the patent's claims to assess infringement, and the production or proximity to it prevents the dispute from being hypothetical or the opinion advisory. In addition, the licensee's real economic interest insures a real and concrete object of the litigation: to

release the licensee from an obligation or liability with respect to an actual or forthcoming product that the patent arguably covers.

The second constitutional limit is "resolvability." A declaratory judgment must be able to resolve the particular, concrete dispute at issue in a way that discourages, if not precludes, further litigation on the same point.

An example may be helpful. Suppose the license at issue covers two patents, a basic patent and an improvement patent, and the licensee's production is still in the planning stage. The licensee thinks it can "invent around" the *improvement* patent, and so requests a declaratory judgment that the *basic* patent is invalid, unenforceable, and not infringed. In the absence of a concrete product in current production, the case would not be ripe for adjudication because the license and royalty obligation might still cover the eventual product by virtue of the improvement patent, even if the basic patent is invalidated. The declaratory judgment would not fully resolve the underlying economic issue: whether the licensee must pay royalties.

Cases like the case at bar, involving substantial current production, are distinguishable. Here there is no question that litigation would determine whether royalties are due with respect to substantial ongoing production of a current product on which the licensed patent's claims can be read. In that respect this case is indistinguishable from an infringement suit by the patentee in the absence of the license, which would also be justiciable.

The last two requirements—for injury in fact and its causation—are the most problematic in this context. If

injury in fact is defined as "invasion of a legally protected interest" (*Lujan*, 505 U.S. at 560) and is taken literally, a strict requirement for it would wipe out most declaratory judgments in patent law, even under the Federal Circuit's test. A "quiescent" patentee who merely owns a patent certainly does nothing to invade a declaratory plaintiff's rights. But neither does a patentee who brings or threatens suit. As long as it acts in good faith or its claim is not baseless, every patentee has a constitutional right[6] to sue and to threaten, immunized from antitrust liability under an entire mini-jurisprudence known as the *Noerr-Pennington* doctrine. *See Professional Real Estate Investors, Inc. v. Columbia Pictures Industries, Inc.*, 508 U.S. 49, 60 (1993) (relaxing *Noerr-Pennington* immunity for a single action only when it is (i) "objectively baseless" and (ii) brought in subjective bad faith); Dratler Licensing, § 2.04[1] (discussing doctrine, its history, and exception).

Since a patentee has every right to threaten and bring suit, its doing so does not invade any protected interest of a licensee or any putative infringer. Therefore, the notion of invading a protected interest as a condition for constitutional standing is far too weak a beam to support declaratory judgments in patent cases.

The gist of the matter is that patent rights are almost always uncertain. Without recognizing that fundamental reality, the doctrine of injury in fact is circular even in pedestrian infringement suits.

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[6] The *Noerr-Pennington* doctrine is ultimately based on the First-Amendment right to petition the government for redress of grievances. *See Eastern R.R. Presidents Conference v. Noerr Motor Freight, Inc.*, 365 U.S. 127, 137, 139 (1961).

An invalid patent cannot be infringed. *See Blonder Tongue*, 402 U.S. at 344, 350. Therefore, whether an infringement defendant's allegedly infringing activities cause injury in fact depends upon whether the patent is valid, which only the litigation itself can resolve. The same circularity exists for declaratory-judgment actions, and therefore there is no reason to distinguish between them insofar as injury in fact or justiciability is concerned.

Only one escape from this conceptual conundrum is evident: recognizing that uncertainty in a patent's validity or enforceability can itself be a cause of injury in fact. *Cf.* Daniel A. Farber, "Uncertainty as a Basis for Standing," 33 Hofstra L. Rev. 1123, 1125-1126 (2005). The ubiquitous uncertainty of patents is indeed a cause of real injury: it motivates licenses to pay real money to avoid horrendous real risks.

Any standing doctrine that refuses to recognize uncertainty as a cause of injury in fact in patent cases must confront the doctrine of *stare decisis*. This Court's very first decision under the Declaratory Judgment Act involved acts that would be difficult, if not impossible, to characterize as "invasion of a legally protected interest." *See Aetna*, 300 U.S. at 237-238, 242 (defendant's formal written claim under insurance policy, asserting that he had become totally disabled and therefore that policy provisions waiving payment of premiums on disability had come into play, supported jurisdiction over insurer's request for declaratory judgment that policies had lapsed for nonpayment). The vast majority of cases in which the Federal Circuit has recognized jurisdiction also involved no

such invasion.[7] Yet the modern doctrine of standing, with its requirement for "injury in fact," developed more than two decades after the Declaratory Judgment Act's adoption. *See* Act of June 14, 1934, ch. 512, 48 Stat. 955; Cass Sunstein, "What's Standing After *Lujan*? Of Citizen Suits, 'Injuries,' and Article III," 91 Mich. L. Rev. 163, 185-186 (1992) (reporting that first appearance of "injury in fact" criterion came in 1958, in treatise on administrative law), citing Kenneth C. Davis, *Administrative Law Treatise* § 22.02, at 211-13 (1958). Proponents of a stricter standing requirement for declaratory judgments based on "injury in fact" therefore must explain how their views avoid canceling an act of Congress and multiple decisions made decades previously.

Both infringement and declaratory-judgment actions in patent cases amply satisfy the real concerns underlying modern standing doctrine. Where they involve current or forthcoming products and nonpretextual economic obligations among parties in privity, they are worlds away from the environmental and social-policy cases in which plaintiffs challenge generally applicable law based on some diffuse "injury" to the environment, good government, or the like. *Cf., e.g., Lujan*, 504 U.S. at 562, 578 (challenge to change in regulation requiring consultation with affected states only for actions affecting endangered-species designations in the United States and on the high seas, but not in foreign countries, failed for lack of showing of injury and redressability); *Sierra Club v. Morton*, 405 U.S. 727, 729-730, 740-741 (1972) (club that challenged Forest

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[7] Most of the Federal Circuit's decisions supporting jurisdiction in patent cases rely on the patentee's charge of infringement or threat of suit—constitutionally protected activity. See Dratler Licensing, § 2.02[1][a][iii][B][I].

Service's lease of public lands to developers of ski resort but did not allege individualized injury to its members lacked standing to sue); *Massachusetts v. Mellon*, 262 U.S. 447, 480, 488-489 (1923) (Court lacks jurisdiction to review allegedly unconstitutional taxation and appropriation at behest of individual taxpayers or State on their behalf).

Just like a patent infringement case, a licensee's declaratory-judgment suit involves a specific and concrete injury (economic loss due to legal uncertainty) to a specific and concrete party (the licensee and declaratory plaintiff), which a declaratory judgment can fully resolve. And just as in a patent infringement suit, a case or controversy exists in an action for declaratory judgment if there is a real or forthcoming product on which to read the patent's claims and a concrete economic interest, such as payment or nonpayment of royalties, that depends on the patent's validity or enforceability or the scope of its claims.[8]

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[8] In this particular case there are additional reasons why a case or controversy existed. In addition to suing for a declaratory judgment that the licensed patent was invalid or unenforceable, Appellant claimed that Respondents had violated the antitrust laws. *See MedImmune*, 427 F.3d at 965-969 (finding these claims also non-justiciable or waived and declining to transfer them to Ninth Circuit). These claims included assertions that: (1) Respondents had colluded with a third party in the patent-interference settlement that presaged issuance of the licensed patent to extend the patent's duration beyond what it would have been absent the settlement and (2) the patent's issuance had resulted from fraud for which Respondents were responsible. See *id.*, 427 F.3d at 965, 967-968. Since the viability of the antitrust claim depended on whether the patent had been procured by fraud and was therefore unenforceable, *see Walker Process Equipment, Inc. v. Food Machinery & Chemical Corp.*, 382 U.S. 172, 175-177 (1965), these collateral claims were substantively intertwined with the request for a declaratory judgment of patent unenforceability.

## CONCLUSION

*Amici* respectfully request that this Court reverse the judgment below, reject the Federal Circuit's "reasonable apprehension of suit" test as inconsistent with the Declaratory Judgment Act and not required by Article III, and announce a new test for the justiciability of declaratory-judgment claims in patent cases along the lines suggested herein.

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(Continued from previous page):

The fact that these claims also were real and concrete and able to be resolved lends weight to the justiciability of the case as a whole. See *MedImmune*, 427 F.3d at 970-971 (opinion dissenting in part, arguing that antitrust claims should be transferred to Ninth Circuit, rather than dismissed). But the justiciability of a request for a declaratory judgment does not depend upon the presence of related claims. It is enough that the claim for a declaratory-judgment itself is real and concrete and that its resolution will have real, concrete and immediate consequences here resolution of the obligation to pay royalties on a product then in current production.

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No. 05-608

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IN THE

# Supreme Court of the United States

MEDIMMUNE, INC.

*Petitioner,*

*v.*

GENENTECH, INC., ET AL.

*ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT*

## BRIEF OF AMICI CURIAE THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK, THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, THE AMERICAN ASSOCIATION OF MEDICAL COLLEGES, THE ASSOCIATION OF AMERICAN UNIVERSITIES AND OTHERS SUPPORTING RESPONDENTS

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## INTEREST OF AMICI CURIAE[1]

Amici and their member universities are non-profit academic institutions that invest significant resources in the scientific research of their faculty, staff and students.[2] The Bayh-Dole Act (P.L. 96-517, Patent and Trademark Law Amendments Act of 1980) encourages such institutions to obtain patent protection for their scientific research and to license those patents to the private sector. This statute has been hailed as "[p]ossibly the most inspired piece of legislation to be enacted in America over the past half-century" because it "unlocked all the inventions and discoveries that had been made in laboratories throughout the United States with the help of taxpayers' money. More than anything, this single policy measure helped to reverse America's precipitous slide into industrial irrelevance." *Innovation's Golden Goose*, THE ECONOMIST'S TECHNOLOGY QUARTERLY (Dec. 2002).

Among the more prominent technological advances made available to the public through Bayh-Dole licensing are the Google and Lycos Internet search engines (Stanford and Carnegie Mellon Universities, respectively); the co-transformation process, a pioneering recombinant DNA technology used to make pharmaceutical products that treat many different diseases and ailments (Columbia University); the cancer drug Taxol (Florida State University); and the nicotine patch (UCLA). *See* Mary Margaret Styer, et al., *A Guide Through the Labyrinth: Evaluating and Negotiating a*

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[1] The parties' letters of consent to the filing of amici briefs have been lodged with the Clerk. Pursuant to Rule 37.6, amici state that no counsel for a party has written this brief in whole or in part and that no person or entity, other than amici, their members, or their counsel, has made a monetary contribution to the preparation or submission of this brief.

[2] A full list of amici filing this brief is set out in Appendix A.

*University Technology Transfer Deal*, 11 B.U. J. SCI. & TECH. L. 221, 222-23 (2005); *Technology Transfer Stories: 25 Innovations that Changed the World*, (2006 ed.) (available at http://www.autm.net/documents/AUTM_BWR.pdf).

Universities use royalty revenue from their licenses to fund further scientific research and educational programs. The continued success of the important national policy embodied in the Bayh-Dole Act depends on the stability of patent licenses, which would be threatened if MedImmune's position were accepted in the present case. In particular, MedImmune's arguments urge an unwarranted expansion of the holding in *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969) that would erode the sanctity of contracts and interfere with vital policies favoring amicable resolution of commercial matters.

Amici The Trustees of Columbia University in the City of New York ("Columbia"), and The Board of Trustees of the Leland Stanford Junior University ("Stanford") have an additional, unique interest in the outcome of this case. They are respondents in *MedImmune, Inc. v. Centocor, Inc., et al.*, No. 05-656, *pet. for cert. filed* Nov. 22, 2005. MedImmune's declaratory judgment action in the *Centocor* litigation was dismissed on the same jurisdictional basis as its complaint in this case; moreover, MedImmune's petition for certiorari in *Centocor* presents the same question as this case. Because MedImmune's actions in *Centocor* strongly highlight the issues underlying the *Genentech* case, Columbia and Stanford are well suited to address the pernicious ramifications of the legal standard MedImmune advocates.

## INTRODUCTION AND STATEMENT OF THE CASE

The Federal Circuit decided *Genentech* on October 18, 2005, subsequent to, and in reliance upon, its decision in

*MedImmune v. Centocor*, 409 F.3d 1376 (Fed. Cir. 2005). MedImmune, however, reversed that chronological order, filing its petition for certiorari in *Genentech* on November 10, 2005, and later petitioning for certiorari in *Centocor* (Nov. 22, 2005). As a result, *Genentech* is before this Court on the merits and the petition in *Centocor* is being held. Despite similar procedural and jurisdictional histories, the facts of the two cases differ. Accordingly, a brief recitation of MedImmune's conduct in *Centocor* should inform any analysis of the practical consequences of the tactics MedImmune asks this Court to condone.

In late 1998, MedImmune approached Columbia seeking a license for U.S. Patent No. 5,807,715 (the '715 patent), which Columbia jointly owns with Stanford. The '715 patent reflects the ground-breaking work of prominent research scientists in the field of monoclonal antibody technology. Columbia referred MedImmune to Centocor, Inc., the exclusive licensee of the '715 patent. Thereafter, MedImmune spent nearly two years negotiating a sublicense with Centocor. During that process, MedImmune analyzed and obtained opinions from multiple law firms about the validity of the patent and whether it covered MedImmune's product Synagis®. MedImmune's negotiating posture included a number of arguments (*e.g.*, patent invalidity and non-infringement) designed to drive down the negotiated royalty rate. Although the universities disagreed with MedImmune's contentions, important concessions were made in order to reach an accord satisfactory to all parties. Ultimately, the sublicense agreement was approved at a reduced royalty rate – less than originally proposed and less than if MedImmune's various contentions had already been rejected in court – and a substantial postponement in the date on which MedImmune's obligation to pay royalties began. *See* 271 F. Supp. 2d 762, 765 (D. Md. 2003).

After signing the sublicense agreement in December 2000, MedImmune began making royalty payments under the '715 patent as of the date specified in the contract. Having resolved all issues with MedImmune, the universities ordered their affairs around the agreed-upon royalty payments, relying on expected revenues to fund further scientific research and educational activities. Unbeknownst to them, however, MedImmune was plotting a very different course. Within days of executing the sublicense agreement, MedImmune sent a copy to its current litigation counsel and began assessing options for a lawsuit. Some fifteen months later, MedImmune first contacted Centocor requesting consent to the cessation of royalties. MedImmune did not identify any meaningful change of circumstances that occurred after it signed the sublicense agreement or any ambiguity in the agreement. Unable to secure Centocor's assent in its newly-proposed non-payment option, and explicitly indicating that it would continue to make the royalty payments specified in the agreement, MedImmune filed a declaratory judgment suit asserting the same invalidity and non-infringement arguments it had raised during the original pre-sublicense negotiations. *See* 409 F.3d at 1378; 271 F. Supp. 2d at 765.

Prior to the Federal Circuit's decision in *Gen-Probe Inc. v. Vysis, Inc.*, 359 F.3d 1376 (Fed. Cir.), *cert. dismissed*, 543 U.S. 941 (2004), Columbia and Stanford filed a motion to dismiss MedImmune's complaint for lack of jurisdiction. Although the motion was initially denied, the district court eventually dismissed the case after *Gen-Probe* was decided. The district court held that where there was a license agreement with which all parties were complying – and expressing their continuing intention to comply – there was no actual controversy under 28 U.S.C. § 2201(a). 2004 U.S. Dist. LEXIS 28800, at **8-9 (D. Md. June 17, 2004).

In affirming, the court of appeals applied its holding in *Gen-Probe* and explained why MedImmune was incorrect in asserting that *Gen-Probe* was inconsistent with Supreme Court and Federal Circuit authority. 409 F.3d at 1379-82. Moreover, the court held that MedImmune "can have no apprehension of suit at all" since "there is nothing for which Centocor can sue MedImmune." *Id.* at 1381. This conclusion follows ineluctably from the fact that "[i]t is undisputed that MedImmune continues to pay timely royalties for Synagis® and is not otherwise in breach of the agreement." *Id.* As the court explained, "a license is, by its nature, an agreement not to litigate. A licensor agrees to receive royalties or other consideration from the licensee in exchange for a covenant not to sue or disturb the licensee's activities." *Id.* at 1379 n.1.

The circumstances of the *Centocor* litigation highlight the more pernicious aspects of the tactics employed by licensees. The licensee in *Centocor* (MedImmune) made the initial approach to the patent owner requesting a license; the licensee sought the license under a patent that had already issued; the parties negotiated and had every opportunity to explore all aspects of their differing views on patent validity and infringement; the parties reached a written accord reflecting a compromise that settled all outstanding issues; there are no changed circumstances subsequent to execution of the agreement; and the licensee continues to enjoy all the benefits of the agreement and, in return, continues to make all royalty payments; the parties remain bound by the contract to which they are adhering.

This brief recitation provides some context for the following arguments against the disruption of established legal relationships that will occur if this Court reverses the judgment and adopts the standard MedImmune urges. These untoward consequences are not merely hypothetical, nor are

they a rhetorical parade of conjured-up horribles. They are the actual circumstances in which Stanford and Columbia were placed by MedImmune's tactics. As a practical matter, they are the inequitable reality any patent holder may face if MedImmune's position is upheld.

## SUMMARY OF ARGUMENT

1. Article III precludes jurisdiction over issues resolved in an ongoing license agreement that all parties continue to honor. Indeed, the licensee here positively insists on maintaining the agreement in force to keep all the benefits for which it bargained. The circumstance of a voluntary, still-operational agreement, with the plaintiff demanding retention of its negotiated shelter, readily distinguishes this case from the two principal authorities being invoked to support Article III jurisdiction: *Altvater v. Freeman*, 319 U.S. 359 (1943), and *Steffel v. Thompson*, 415 U.S. 452 (1974). This circumstance also defeats the licensee's ability to meet several established Article III requirements.

At the core of its argument, MedImmune urges an extension of *Lear* to entitle a licensee, asymmetrically, to press its challenges while retaining the benefits of its license without the risks faced by an infringer. But *Lear* merely protected a licensee who faced actual litigation commenced by the licensor; it did so by permitting a full range of defenses, including the defense of patent invalidity. MedImmune seeks to transform that limited protection into an offensive weapon for licensees to wield against licensors at any time. *Lear* does not compel that result; nor does the rationale of *Lear* support it. Just as the Court has previously refused to extend *Lear*, it should do so again now.

In fact, even if the express policy underpinning of *Lear* – promoting prompt adjudication of patent validity – is

viewed (incorrectly) as the only policy relevant to the question, that policy itself is contrary to MedImmune's contention. MedImmune's argument would permit a prospective licensee to forgo all pre-agreement opportunities to litigate patent validity, to enter into a negotiated resolution of all outstanding issues (including patent validity), and to wait years before launching litigation against a patent holder who made substantial concessions in the original agreement and has no recourse against the belatedly litigious licensee.

2. The rule MedImmune advocates assumes that in the circumstances presented in this case, federal patent law displaces valid contracts that are fully enforceable under state law. MedImmune's contention is wrong as a matter of federalism and general patent law, and especially so in the context of universities fulfilling the statutory mission of the Bayh-Dole Act. The invaluable benefits that the Act has achieved (encouraging inventions by university researchers to benefit the public) would be drastically curtailed if licensors lose the repose that their contractual agreements were intended to produce. Under MedImmune's approach, substantial litigation expenses would have to be built into the royalty calculations of license agreements, thus raising the cost of providing breakthrough technology to the public.

3. Even if Article III requirements could be satisfied by a plaintiff in MedImmune's position, a declaratory judgment action should not be allowed to proceed. The standard employed by the Federal Circuit in cases where license agreements remain operational, is an appropriate guideline for district courts asked to entertain claims under the Declaratory Judgment Act. Indeed, the line drawn by the Federal Circuit is consistent with this Court's precedents, with the need to consider the public interest, and with the practical exigencies of the world of commerce.

## ARGUMENT

### I. A LICENSEE'S CONTINUING, VOLUNTARY PERFORMANCE OF ITS AGREEMENT TO PAY PATENT ROYALTIES BARS ARTICLE III JURISDICTION OVER THE LICENSEE'S DECLARATORY JUDGMENT CHALLENGE TO THE PATENT'S VALIDITY, ENFORCEABILITY, OR COVERAGE

#### A. Traditional Article III Standards Preclude Jurisdiction

"'[N]o principle is more fundamental to the judiciary's proper role in our system of government than the constitutional limitation of federal-court jurisdiction to actual cases or controversies.'" *DaimlerChrysler Corp. v. Cuno*, 126 S. Ct. 1854, 1861 (2006) (quotation omitted). This principle "is as true of declaratory judgments as any other field." *United Pub. Workers v. Mitchell*, 330 U.S. 75, 89 (1947); *accord U.S. Nat'l Bank of Oregon v. Indep. Ins. Agents of Am.*, 508 U.S. 439, 446 (1993).

The Court has elaborated the constitutional requirements through a number of overlapping doctrines. *See Allen v. Wright*, 468 U.S. 737, 750 (1984). Because of that overlap, there are multiple doctrinal ways of identifying the fundamental problem presented by suits filed by licensees who continue to perform under operational agreements: plaintiff voluntarily entered into an agreement that affords substantial benefits that it positively insists on retaining even while it litigates. This amicus brief does not exhaustively explore all the ways in which this core fact defeats Article III jurisdiction. Instead, this brief explains why a selected few of the established Article III requirements cannot be met by a

licensee like MedImmune while it enjoys the self-protection afforded by the license agreement.

At the outset, it is clear that neither of the two principal authorities invoked to support Article III jurisdiction involves the distinctive feature of the present case – plaintiff's continuing, voluntary performance of an operative agreement it seeks to maintain. Neither *Altvater* nor *Steffel* involved an unquestionably valid agreement which both parties were performing without breach. In *Altvater*, there was no license. The agreement had already been terminated, the patentee had sued for infringement and other claims, and the licensee's continuing payment of royalties was wholly *involuntary*, "under the compulsion of an injunction decree." 319 U.S. at 365. In *Steffel*, there was plainly no agreement by the plaintiff not to distribute protest handbills on private property. He ceased the protest activities under "a genuine threat of enforcement" of a state criminal trespass statute. 415 U.S. at 475. The parties also stipulated that if plaintiff engaged in such conduct "a warrant would be sworn out" and he would be arrested. *Id.* at 456 & n.4. By no stretch of the imagination is MedImmune's voluntary performance of its agreement comparable to compliance with a coercive injunction (*Altvater*) or forbearance under a genuine threat of criminal prosecution (*Steffel*).

For Article III jurisdiction to exist, plaintiff must show: a legally cognizable "injury in fact" (1) that is "concrete and particularized," (2) that is "fairly traceable" to the defendant's action, and (3) that can be redressed by a favorable judicial decision. *McConnell v. FEC*, 540 U.S. 93, 225-27 (2003); *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560-61 (1992); *Allen*, 468 U.S. at 751-52, 755-59. A plaintiff must "show that there is a substantial controversy, between parties having adverse legal interests, *of sufficient immediacy and reality* to warrant the issuance of a

declaratory judgment." *Md. Cas. Co. v. Pac. Coal & Oil Co.*, 312 U.S. 270, 273 (1941); *Whitmore v. Arkansas*, 495 U.S. 149, 155, 158 (1990); *City of Los Angeles v. Lyons*, 461 U.S. 95, 101 (1983). In various ways, suits like MedImmune's fall short under these standards.

The situation presented by MedImmune's agreement with the respondents – and even more starkly by its agreement with Centocor – is a common one, replicated in the daily routine of patent licensing that spreads technology throughout the economy. A patentee and a firm wanting to engage in conduct arguably covered by a patent enter into an extended negotiation about whether the conduct is covered and whether the patent is a valid, enforceable one. In that negotiation, they press their respective views and also consider the costs (*e.g.*, in money, delay, distraction of personnel) of litigating the dispute to a judicial resolution. Often, they including a desire to avoid the costs of litigation, they reach an agreement in which the amount paid reflects assessments of likely litigation outcomes: more than if the licensee were to prevail in court; less than if the patentee were to prevail in court. The licensee gets substantial benefits: the right to practice the patent free of litigation threat; the freedom to do so immediately without awaiting years of litigation; and a negotiated royalty rate reduced from the patentee's initial offer to reflect any perceived uncertainty over issues of patent validity, enforceability, and coverage. Indeed, the very point of the agreement is to settle the dispute and to put the technology into practice without wasteful expenditures on judicial processes.

The post-agreement state of repose is inherent in the parties' arrangement and derives from the options facing potential licensees: "to use the rights under a license, to not use the rights (and avoid any need for a license), or to use the rights without a license and litigate any infringement claim."

John W. Schlicher, LICENSING INTELLECTUAL PROPERTY: LEGAL, BUSINESS, AND MARKET DYNAMICS 48 (1996). Once the prospective licensees opt to execute negotiated agreements, their licenses "are often best viewed as settlements of potential future litigation." *Id.* at 49.

There is a fatal tension between the Article III requirements of a live controversy of sufficient immediacy and reality (injury-in-fact, traceability, redressability) and the absence of any potential liability for infringement during the full term of a license agreement as the licensee enjoys immunity from any such claim. *See De Forest Radio Tel. Co. v. United States*, 273 U.S. 236, 241 (1927). Licensees who make timely payments under their agreements not only lack any present threat of an infringement claim, but also enjoy a binding contractual promise barring precisely that claim. *See* Kim R. Smith, *Foreclosure of License Validity Challenges with Procedural Barriers*, 61 J. PAT. OFF. SOC'Y 690, 701 (1979); Note, *Patent Licensee Standing and the Declaratory Judgment Act*, 83 COLUM. L. REV. 186, 197 (1983). Moreover, if the licensee stops performing under the agreement and is sued for breach, there is no impediment to the defense of patent invalidity. *Lear*, 395 U.S. 653. Should another party successfully challenge the patent's validity, the royalty obligation would cease. *Id.* And, if the licensee learns of any reason to doubt the patent's validity because of prior art it can commence a re-examination proceeding at the Patent and Trademark Office ("P.T.O.") while still honoring its obligation to pay royalties. 35 U.S.C. §§ 301-307.

The lack of Article III jurisdiction in this case fits within several well-established jurisdictional categories. For example, the licensee is fairly viewed as failing to meet the threshold requirement of legally cognizable injury. When a party has made an exchange for equal value, it has not suffered a harm. *See Dura Pharms., Inc. v. Broudo*, 544 U.S.

336, 342 (2005) ("as a matter of pure logic, at the moment the transaction takes place, the plaintiff has suffered no loss; the inflated purchase payment is offset by ownership of a share that at that instant possesses equivalent value"). When a licensee like MedImmune enters into its license agreement, it receives what it has judged to be equal value in return for its payment: freedom from suit and from the risk of an injunction against its business and from a much higher royalty rate should any uncertainties about the validity, enforceability and coverage be resolved in favor of the patentee. As long as the licensee retains those benefits, it keeps the agreed-upon equivalent of the payment obligation about which it seeks to complain. Of course, repudiation would eliminate that equal value, as in *Lear*. But without repudiation, the licensee suffers no cognizable harm.

MedImmune's argument also may be viewed as foundering on the causation requirement of an injury traceable to the defendant's action. Its claimed injury – payment of royalties for practicing the patents – was a voluntary obligation undertaken in light of the usual business and legal uncertainties. That act, like the act of a third party, breaks the chain of causation leading back to the licensor. Distinctions of this sort are commonplace in causation analysis and echo the distinction that, in a different context, informed the plurality opinion in *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 525-26 (1992) (Stevens, J.) (noting difference between express warranty claims imposed under State law and those imposed "*by the warrantor*").

MedImmune's claim can also be seen as failing the Article III justiciability standard in another critical respect. The interest MedImmune asserts – cessation of agreed upon payments – is entirely dependent on the lawsuit. After all, the obligation arose from MedImmune's voluntary agreement, and would end (during the prescribed term of the

license) only as a result of the litigation. But this Court has held that "an interest that is merely a 'byproduct' of the suit itself cannot give rise to a cognizable injury in fact for Article III standing purposes." *Vermont Agency of Natural Res. v. U.S. ex rel. Stevens*, 529 U.S. 765, 773 (2000). That principle is fully applicable here, where MedImmune's alleged injury is necessarily framed in terms of the result in the lawsuit.

Finally, these circumstances also fit within another established category in which Article III jurisdiction is lacking. This Court has made clear that a valid state law bar to the relief sought – an "adequate and independent state ground" – eliminates Article III jurisdiction to hear a federal-law claim. *See Coleman v. Thompson*, 501 U.S. 722 (1991); *Ake v. Oklahoma*, 470 U.S. 68, 75 (1985); *Herb v. Pitcairn*, 324 U.S. 117, 126 (1945); *Enter. Irrigation Dist. v. Farmers Mut. Canal Co.*, 243 U.S. 157, 164 (1917). Although stated in terms of this Court's review of state court judgments, the principle is not in any way dependent on the language of 28 U.S.C. § 1257. The operative principle is that there is no case or controversy if state law validly bars relief sought in federal court. One kind of state ground that can be adequate and independent is a waiver or other forfeiture, such as a procedural default. *See Louisville & Nashville R.R. v. Woodford*, 234 U.S. 47, 51 (1914); Richard H. Fallon Jr., et al., HART AND WECHSLER'S THE FEDERAL COURTS AND THE FEDERAL SYSTEM 525 n.2 (4th ed. 1996) ("[t]he same principle operates when there is an antecedent state law *procedural* ground – ordinarily that the party seeking Supreme Court review failed to raise the federal question in accordance with state procedural rules").

Similarly, in this case (and in *Centocor*) MedImmune does not suggest that its agreements are invalid in any way. The sole basis, therefore, on which MedImmune seeks to

cease paying royalties is by federal preemption of contracts whose validity and enforceability are unquestioned under state law. Under this analytical framework, therefore, the ultimate jurisdictional issue turns on the preemption question. From that perspective, it should be clear that MedImmune's position cannot prevail, especially where it is *relying* on the same license as enforceable under state law – paying royalties and obtaining all the benefits for which it bargained (including the right to use the patented invention, immunity from a claim of infringement, treble damages and attorneys' fees; and, in return, all the favorable consequences of being the first to market).

### B. Federal Law Respects the Licensor's Repose While the Licensee is Sheltered by the License

A contract creates repose that should preclude federal jurisdiction as long as no party is threatening to terminate the agreement. At the core of the argument of MedImmune and its amici is the submission that federal patent policy upsets, rather than respects, this repose by allowing a challenge to the patent's validity, enforceability, or coverage, even while the licensee maintains the benefits of the license. This Court should reject that submission. A licensee who chooses to maintain the shelter of the license has no standing to contest the repose that is the essence of the agreement.

#### 1. *Lear* Does Not Authorize a Challenge to Patent Validity in These Circumstances

The principal basis upon which MedImmune argues that federal patent law should control rests on *Lear*. Much of MedImmune's argument, however, is premised on a misreading of *Lear*, coupled with a misguided effort to expand *Lear* well beyond its limited scope. Before *Lear*,

licensors had considerable power over their licensees, including the doctrine of licensee estoppel that precluded a licensee from challenging the validity of the license – even to defend a breach of contract suit by the patentee. *Lear* abolished the licensee estoppel doctrine to provide patent licensees with a full range of defenses and established a particular measure of parity between the legal arsenals of licensees and patent holders. *See* 395 U.S. at 657.

MedImmune now wishes to transmogrify the protection afforded by *Lear* into an equilibrium-destroying weapon to give licensees an unfettered right to challenge a patent even as they continue to enjoy the contractual right to practice that patent and retain the other benefits of the license. *Lear* never contemplated such a situation. *See, e.g.*, William C. Rooklidge, *Licensee Validity Challenges and the Obligation to Pay Accrued Royalties:* Lear v. Adkins *Revisited (Part II)*, 69 J. PAT. & TRADEMARK OFF. SOC'Y 5, 10 (1987) ("If the licensee filed a declaratory judgment action without repudiation, there should be no jurisdiction because of a lack of 'a case or controversy.' The Supreme Court in *Lear* did not write that requirement out of the Declaratory Judgment Act"). Indeed, as pointed out in Justice White's concurrence, the *Lear* licensee "concede[d] that it would be estopped to contest the validity of any patent issued to Adkins . . . so long as it continued to operate under that agreement." 395 U.S. at 679 n.1 (quoting *Adkins v. Lear, Inc.*, 52 Cal. Rptr. 795, 805 (Cal. App. 1996)).

The licensee in *Lear* stopped paying royalties three years prior to the commencement of suit by the patentee. *See* 395 U.S. at 661-62. Hence, unlike the instant case, "a controversy existed in the *Lear* case." Note, *Patent Licensee Standing*, 83 COLUM. L. REV. at 200. All *Lear* held was that a licensee could raise a defense of patent invalidity when sued in state court by a patentee for royalties due. *See id.* at

200-01. MedImmune and its amici incorrectly equate the absence of estoppel (*Lear*), with the presence of a justiciable controversy. *Lear*, which did not involve any Article III issue, neither requires nor even supports that conclusion.

Aside from the dispositive factual differences between this case and *Lear*, there are additional reasons why *Lear* should not be extended to reach the facts presented here. *Lear*, decided the same Term as *Fortner I*, has been described as the apex of an "anti-patent anti-monopoly" milieu. Rooklidge, *Licensee Validity Challenges* 69 J. PAT. & TRADEMARK OFF. SOC'Y 5 at 15 & n.22; Rochelle Cooper Dreyfuss, *Dethroning* Lear: *Licensee Estoppel and the Incentive to Innovate*, 72 VA. L. REV. 677, 724 (1986). In the intervening four decades, the Court has employed more discerning analyses in both areas of law. *See, e.g., Ill. Tool Works, Inc. v. Indep. Ink, Inc.*, 126 S. Ct. 1281, 1289-92 (2006). That is good reason not to extend *Lear*.

Indeed, the Court has already declined to extend *Lear*. In *Aronson v. Quick Point Pencil Co.*, 440 U.S. 257 (1979), the Court held that federal patent law does not preempt the enforcement of a contract valid under state law. Although *Aronson*'s facts differ from those here, the Court's opinion is instructive. The parties entered into a licensing agreement while a patent application was pending, specifying that the royalty rate would drop if the patent application was not allowed within five years. When the patent did not issue by the prescribed time (it was subsequently rejected by the Patent and Trademark Office), the licensee continued to pay royalties at the reduced rate for 14 years. By then, rivals with no obligation to pay royalties had entered the market and the licensee refused to make further payments. *See Quick Point Pencil Co. v. Aronson*, 425 F. Supp. 600, 601 (E.D. Mo. 1976). The licensee subsequently sued for a declaratory judgment, claiming that "state law which might otherwise

make the contract enforceable, was pre-empted by federal patent law." 440 U.S. at 260. Relying on *Kewanee Oil* and *Brulotte v. Thys Co.*, the Court rejected the licensee's claim, holding that "[s]tate law is not displaced merely because the contract relates to intellectual property which may or may not be patentable." *Id.* at 262. The Court noted that the parties had contracted with "full awareness of . . . the possibility that a patent might not issue." *Id.* at 261. Of even additional importance for present purposes, *Aronson* concluded that "neither the holding nor the rationale of *Lear*" controlled in those circumstances. *Id.* at 264. Forgoing an opportunity to extend *Lear*, the Court recognized that there were valid economic reasons why a firm would be willing to "pay for the opportunity to be first in the market" even in the absence of a valid patent or trade secret, and that "[f]ederal patent law is not a barrier to such a contract." *Id.* at 266.

Today, and in the circumstances presented by MedImmune, there is even less justification to extend *Lear*. First, even at the time of *Lear*, the value of clearing away bad patents was dominant (over policies favoring licensing, litigation avoidance, and respect for contracts) only where litigation was already underway and the contract was no longer being respected. There is no reason to apply *Lear*'s balance when the licensee insists on continued operation of the contract. More generally, since *Lear* this Court has taken a less one-sided view of the multiple policies underlying federal law affecting intellectual property, as reflected in *Kewanee Oil*, *Aronson* and *Illinois Tool*. *See also AirLine Pilots Ass'n, Int'l v. O'Neill*, 499 U.S. 65, 78 (1991) (policy favoring contractual resolution of labor disputes).

Even as to the policy that *Lear* emphasized, the statutory law has been changed in a vital respect. Amendments subsequent to *Lear* provide that any party may request a re-examination by the P.T.O. 35 U.S.C. §§ 301-

307. Accordingly, *Lear*'s concern for resolution of patent validity issues would not be thwarted if this Court affirms the judgment in this case.

Further, to the substantial extent that *Lear* was expressly premised on a policy of promoting prompt adjudication of patent validity (395 U.S. at 673-74), that policy is not advanced in the slightest by conferring on licensees an open-ended opportunity to challenge patent validity at any time during the term of the license agreement. *See, e.g., Centocor*, 409 F.3d at 1377-78 (MedImmune waited sixteen months after license before suing); *cf. Aro Corp. v. Allied Witan Co.*, 531 F.2d 1368, 1373 (6th Cir. 1976) (Markey, C.J., sitting by designation) ("Whatever boon *Lear* may have provided those who take licenses under certain conditions, it cannot be interpreted so broadly as to condone a kind of gamesmanship, wherein an alleged infringer, after employing the judicial system for months of discovery, negotiation, and sparring, abandons its challenge to validity, executes a license in settlement, and then repudiates the license and seeks to start the fight all over again in the courts"). To the contrary, it is far more consistent with the policy articulated in *Lear* to respect operative licenses by barring the licensee's suit. Doing so encourages potential licensees to seek judicial resolution of validity issues *before* entering a license agreement. *See* Dreyfuss, *Dethroning* Lear, 72 VA. L. REV. at 722 ("[T]he right to challenge validity, standing alone, will not stimulate early patent challenges. Rather, that incentive is better furnished by a rule that warns licensees that if they do not challenge at first opportunity, they may lose that right forever"); Schlicher, *A Lear v. Adkins Allegory*, 68 J. PAT & TRADEMARK OFF. SOC'Y 427 (1986).

### 2. Federal Patent Law Should Respect, Not Preempt, License Agreements Like MedImmune's

There are also compelling affirmative reasons why, in the circumstances presented here, federal patent law should not preempt operative contracts. First, as a matter of federalism, there is a general presumption against preemption, and intellectual property cases reflect this principle. *See, e.g., Brulotte, Kewanee, Aronson.* Second, the presumption is fortified here by the patent statute's long-accepted protection of a patentee's broad freedom to parcel out its exclusivity rights as it chooses (subject to very limited constraints). *See, e.g., Zenith Radio Corp. v. Hazeltine*, 395 U.S. 100, 135-36 (1969); *Cont'l Paper Bag Co. v. Eastern Paper Bag Co.*, 210 U.S. 405, 423-25 (1908); *Bement v. Nat'l Harrow Co.*, 186 U.S. 70, 88-91 (1902).

Preemption in these circumstances would adversely affect patent licensing, which fosters competition and economic growth and efficiency by making technology and intellectual property more widely available. *See* Note, *Patent Licensee Standing*, 83 COLUM. L. REV. at 206 ("[i]f current licensees are allowed to bring offensive patent validity challenges, the patent system may be injured. Injury to the patent system may, in turn, harm our long-standing policy of promoting invention, and may ultimately reduce both competition and technological advance"); 7 PAT. L. PERSP. § 12.4[6] (Matthew Bender 2d ed. 2005) at 12-123 ("[W]e may see a major contraction in the number of licenses granted"). Indeed, unrestricted licensee suits would burden patentees whose "constitutionally recognized property right may become too expensive to maintain" and would "ultimately result in higher costs as patentees increase their fees to cover anticipated litigation expenses." *See* Note, *Patent Licensee Standing*, 83 COLUM. L. REV. at 192, 211. These costs will

undoubtedly be passed along to the public, "thus diminishing the benefits the public currently receives from the patent system." *Id.*; *see also* Emmette F. Hale, III, *The "Arising Under" Jurisdiction of the Federal Circuit: An Opportunity for Uniformity in Patent Law*, 14 FLA. ST. U. L. REV. 229, 259 (1986) (making same point). Many useful technologies are licensed by universities for relatively small financial returns; the prospect of expensive patent litigation would at a minimum raise the cost of making these inventions available to the public.

Alternatively, prospective licensors would seek to ensure the benefit of their bargain by filing an infringement suit first and then entering into a license agreement as part of a consent decree. *See* 7 PAT. L. PERSP. § 12.4[6] at 12-124. Licensors would thereby obtain the benefit of *res judicata* with respect to the licensees' patent validity claims. *See Foster v. Hallco Mfg. Co.*, 947 F.2d 469, 476-77 (Fed. Cir. 1991); *Buckley v. Airshield Corp.*, 977 F. Supp. 375, 377-78 (D. Md. 1997). Encouraging licensors to file such plainly unnecessary suits whenever they consider granting a license would be detrimental in obvious ways to the judicial system, the patent system, and the flow of commerce.

### 3. The Policy Considerations are Reinforced in the University Setting By the Bayh-Dole Act

The adverse consequences of MedImmune's arguments in this case would be particularly damaging to educational institutions that support scientific innovation in the United States by reinvesting royalty payments in further research and educational activities. *Cf. eBay Inc. v. MercExchange, L.L.C.*, 126 S. Ct. 1837, 1840 (2006) (noting that most university researchers prefer to license their patents rather than obtain financing to market inventions

themselves). As universities, public and private, divert funds from research and educational programs to combat the licensee gamesmanship MedImmune urges, the licensees face no commensurate risk. That result is plainly contrary to the public interest (especially when taxpayer money is being diverted from research) and, more specifically, to the important national policy embodied in the Bayh-Dole Act.

That Act is designed to promote the transfer of useful (and often ground-breaking) technology from non-profit research institutions to the public. As Congress understood, special circumstances characterize the reality of patent licensing by universities. First, universities lack the internal capacity to bring their inventions to market. They are not commercial institutions; they have no manufacturing capability; and their financial resources are dedicated to educational and research purposes. As a consequence, all prospects for commercial application of the patents must come from the licensee; this reality gives the prospective licensee greater leverage than it would enjoy in negotiations with a commercial patentee.

Second, many universities do not have sufficient litigation budgets to spend the millions necessary to defend their patents. The need for true patent peace with licensees is therefore particularly compelling in this context, a point that is underscored by the significant technology transfers from institutions with relatively modest endowments and financial resources. Major advances in genetic research flowed from inventions licensed by Tufts University (Bead Away technology that helps analyze genetic variation and function) and the University of Maryland, Baltimore County (Cell station reactor that speeds the discovery and process development stages of fermentation and culture-based medical products). Researchers at North Dakota State University invented an additive for weed control that reduces

farmer's costs by half. New technology developed at the University of Akron eases eye strain from viewing computer monitors and other consumer products. Under the regime MedImmune posits, costs would skyrocket for providing the public with the benefit of these and hundreds of other inventions in fields such as agriculture, biotechnology, computer science, health, medicine, safety, nanotechnology and the environment. *See generally Technology Transfer Works: 100 Cases from Research to Realization* (2006) http://www.autm.net/documents/06ReportsFromField.pdf. Because the Bayh-Dole Act expresses so clear a mandate to promote the efficient transfer of technology for public benefit, it reinforces the view that, at least in the university setting, no expansive preemption implications can be drawn from the Patent Act.

When the practical realities of the licensing arrangement are properly understood, it is evident that Article III would not permit a lawsuit commenced by a party adhering to a binding resolution of the very issue it seeks to litigate. For just this reason, the line drawn by the Federal Circuit comports with established Article III jurisprudence because it accurately reflects the fact that at the crucial time (*i.e.*, the date a complaint is filed), the licensee is fully protected by the agreement it voluntarily entered and continues to honor. Whether viewed under the rubric of standing, injury, traceability or causation, a licensee in good standing therefore falls outside the ambit of Article III.

## II. EVEN IF MEDIMMUNE'S SUIT PRESENTED A CASE OR CONTROVERSY, IT SEEKS EQUITABLE RELIEF THAT SHOULD BE CATEGORICALLY UNAVAILABLE UNDER THE DECLARATORY JUDGMENT ACT

The absence of a live case or controversy should bring the analysis to a close with the Federal Circuit's standard upheld. Surely that should be the case when, as in *Centocor*, the patent issued prior to the license, the licensee had ample opportunity to review and assess the patent (and did so, with multiple opinions of counsel), and the licensee obtained substantial concessions on timing and amount of royalty payments during negotiations that culminated in the resolution set forth in the license agreement.

This Court has long recognized that the Declaratory Judgment Act "was an authorization, not a command. It gave the federal courts competence to make a declaration of rights; it did not impose a duty to do so." *Public Affairs Assocs., Inc. v. Rickover*, 369 U.S. 111, 112 (1962). Thus, in assessing a declaratory judgment claim, "[i]t is always the duty of a court of equity to strike a proper balance between the needs of the plaintiff and the consequences of giving the desired relief." *Eccles v. Peoples Bank of Lakewood Village*, 333 U.S. 426, 431-32 (1948). Recognizing that the Act "created an opportunity, rather than a duty, to grant a new form of relief to qualifying litigants" (*Wilton v. Seven Falls Co.*, 515 U.S. 277, 288 (1995)), the Court has expressly endorsed the views of Professor Edwin Borchard, the acknowledged author of the Act (*id.*):

> We agree, for all practical purposes, with Professor Borchard, who observed half a century ago that "there is . . . nothing automatic or obligatory about the assumption of 'jurisdiction' by a federal court"

to hear a declaratory judgment action. Borchard, DECLARATORY JUDGMENTS, at 313.

Inherent in the grant of discretionary authority to issue declaratory relief is the companion authority for appellate courts to set appropriate boundaries for the exercise of that discretion. In the absence of limits and standards, discretion would devolve into random, even arbitrary, decisions that would diminish the public's ability to assess precedent as a guide to conduct. Any semblance of predictability, or instruction for ordering one's affairs, would be lost. But, this Court has stoutly resisted the notion that discretion should drift into a regime of random decisionmaking. Where a trial court exercises discretion, its "judgment is to be guided by sound legal principles" because "[d]iscretion is not whim, and limiting discretion according to legal standards helps promote the basic principle of justice that like cases should be decided alike." *Martin v. Franklin Capital Corp.*, 126 S. Ct. 704, 710 (2005) (quoting *United States v. Burr*, 25 F. Cas. 30, 35 (C.C. D. Va. 1807) (Marshall, C.J.)); *cf.* Henry J. Friendly, *Indiscretion About Discretion*, 31 EMORY L.J. 747, 771-73 (1982). Lower courts' discretion is necessarily constrained by accumulated precedent, by guidelines established in appellate decisions, and by the mandate that courts "must also take account of the public interest." *U.S. Bancorp Mortgage Co. v. Bonner Mall P'ship*, 513 U.S. 18, 26 (1994). Assessment of the public interest results in the articulation of general rules that govern the lower courts, a course this Court follows in multiple contexts. *E.g.*, *Martin*, 126 S. Ct. at 710; *Wilton v. Seven Falls Co.*, 515 U.S. 277, 288 (1995); *Albemarle Paper Co. v. Moody*, 422 U.S. 405, 416, 422 (1975).[3]

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[3] *See also Local 28 of the Sheet Metal Workers' Int'l Assoc. v. EEOC*, 478 U.S. 421, 475 (1986) ("While the fashioning of 'appropriate'

In the operative-license context, the Federal Circuit standard articulated in *Gen-Probe*, *Centocor*, and *Genentech* is the most appropriate one for the exigencies of patent licensing. The standard serves Article III principles, general principles governing the availability of judicial relief, and the policies specific to the patent context. *See* pages 8-20 *supra*.

The Federal Circuit standard is directly rooted in Article III tenets (even if, as this portion of the brief assumes, Article III does not of its own force *require* this standard). *See* pages 8-14 *supra*; *see also Babbitt v. United Farm Workers Nat'l Union*, 442 U.S. 289, 298-99 (1979) (Article III requires plaintiff to show "credible" threat of prosecution before challenging statute); *Younger v. Harris*, 401 U.S. 37, 42 (1971) ("persons having no fears of state prosecution except those that are imaginary or speculative, are not to be accepted as appropriate plaintiffs"); *Golden v. Zwickler*, 394 U.S. 103, 109-10 (1969) (plaintiff must show that threat of prosecution is real and immediate before challenging validity

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remedies for a particular Title VII violation invokes the 'equitable discretion of the district courts,' we emphasize that a court's judgment should be guided by sound legal principles. In particular, the court should exercise its discretion with an eye towards Congress' concern that race-conscious affirmative measures not be invoked simply to create a racially balanced work force.") (quotation omitted); *Ford Motor Co. v. EEOC*, 458 U.S. 219, 227 (1982) ("[W]hen Congress invokes the Chancellor's conscience to further transcendent legislative purposes, *what is required is the principled application of standards consistent with those purposes* and not equity [which] varies like the Chancellor's foot.") (emphasis added; quotation omitted); *United States v. Criden*, 648 F.2d 814, 818 (3d Cir. 1981) ("[T]he contours of a guiding rule or even principle may develop as the courts begin to identify the policies which should control. Thus, for example, although the selection of an appropriate remedy has been generally deemed to lie in the equitable discretion of the trial judge, *after experience has accumulated the appellate courts may decide that a specific remedy should be awarded as a general rule*") (emphasis added).

of statute). Even if, *arguendo*, Congress could press the limits of Article III and constitutionally provide for declaratory judgment suits in circumstances like this, the Federal Circuit bar on such suits is a proper standard limiting the exercise of equitable authority under the Declaratory Judgment Act at least until Congress speaks to the contrary.

A rule denying relief in the present circumstances also reflects the broadly applicable principle that a claimant's voluntary act may operate to disentitle him to relief. *See U.S. Bancorp*, 513 U.S. at 25 ("'a suitor's conduct in relation to the matter at hand may disentitle him to the relief he seeks'") (quoting *Sanders v. United States*, 373 U.S. 1, 17 (1963) and citing *Fay v. Noia*, 372 U.S. 391, 438 (1963)). The Court recently applied this principle in the context of appellate jurisdiction. *Unitherm Food Systems, Inc. v. Swift-Eckrich, Inc.*, 126 S. Ct. 980, 988 (2006), held that a court of appeals is "powerless" to grant relief a party chose to forgo in the district court. The analysis in *Unitherm* was informed by the statement in *Yakus v. United States*, 321 U.S. 414, 444 (1944), that "[n]o procedural principle is more familiar to this Court than that a . . . right may be forfeited . . . by the failure to make timely assertion of the right before a tribunal having jurisdiction to determine it." (*quoted in Unitherm*, 126 S. Ct. at 988). A prospective licensee who opts to resolve outstanding issues with the patent holder rather than pursue prompt pre-license judicial resolution should similarly leave the courts powerless to entertain belated efforts to obtain relief the licensee chose previously to forgo.

In the patent setting, precluding suit when a license remains operative faithfully embodies Professor Borchard's views on the availability of declaratory remedies in patent cases. His treatise's chapter on "Patents" contains a sub-section entitled "Cases or Controversies," which advises that "a patentee's claim of infringement is a condition precedent"

of a declaratory judgment action challenging validity. Edwin Borchard, DECLARATORY JUDGMENTS 807 (2d ed. 1941).[4] This commentary provides the short and complete answer to MedImmune's contention that the Act's drafters could not have imagined that a holder of a valid license lacked an actual case or controversy. Pet. Br. 12, 28-31.

Additional public policy factors weigh decisively in favor of the Federal Circuit rule against declaratory judgment actions by licensees in good standing. For many licenses, the patent granted by the P.T.O. is available for the public to examine in its final form before the parties commence their license negotiations. The prospective licensee thus has the ability to study the patent's claims, including its validity and scope, and to obtain an opinion of counsel. The prospective licensee then makes a business decision weighing the cost of accepting a license and paying royalties against the benefit of

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[4] Professor Borchard explained at greater length (*id.*; emphases added):

> [I]t seems best to *limit declaratory relief for the infringer to cases in which an adversary claim has been made against him*, though it may, it is believed, apply to an article not yet manufactured but only about to be manufactured. This requirement, present in practically all the adjudicated cases, refutes the fear that patentees might be harassed by prospective infringers and be obliged continually to defend their patents. *The fact that a patentee's claim of infringement is a condition precedent of this type of action* places the matter of adjudication of the patent within the control of the patentee, for, if he wishes to avoid adjudication, he can refrain from making charges of infringement. But having made the charge, he then exposes himself to adjudication. In other words, the mere existence of the patent is not a cloud on title, enabling any apprehensive manufacturer to remove it by suit. *It requires an assertion of right under the patent to place the alleged infringer in gear to join issue and challenge the title.*

eliminating the litigation risk that the patent will be found valid and infringed by the licensee's product. *See* Schlicher, LICENSING INTELLECTUAL PROPERTY at 48.

MedImmune's arguments will shatter the equilibrium in patent license agreements in a disruptive way that unfairly favors patent licensees. Under MedImmune's position, licensors will lose rights to continued royalty payments with no chance of recovering any concessions they made during license negotiations. However, the licensee risks nothing to challenge the patent other than its litigation costs. Even if the challenge fails, the licensee continues to enjoy the same immunities and benefits under the license agreement at the same royalty rate. In contrast to MedImmune's contention, the neutral approach taken by the Federal Circuit in *Gen-Probe, Centocor, Genentech,* and *C.R. Bard, Inc. v. Schwartz,* 716 F.2d 874 (Fed. Cir. 1983) preserves the balance of benefits set forth in license agreements.

Neither MedImmune nor its amici supporters identify any compelling public policy reason to afford patent licensees such a uniquely harmful advantage. In fact, there is no equitable basis to allow licensees to maintain the benefits of their license at the same time that they are trying to take away the rights of the licensor. *See generally* Nellie A. Fisher, *The Licensee's Choice: Mechanics of Successfully Challenging a Patent Under License,* 6 TEX. INTELL. PROP. L.J. 1, 43 (1997) ("the licensee who elects to pay royalties while challenging the patent's validity is in effect 'having its cake and eating it too'"); 4 PAT. L. PERSP. § 6.2[2.-2], at 6-41 ("There is "no reason to let the licensee have the best of both worlds. To do so permits him to litigate validity with total immunity from the normal consequences of a holding that a patent is valid and infringed"); *cf. Kelly v. Kosuga,* 358 U.S. 516, 520-21 (1959) ("[T]he courts are to be guided by the overriding general policy, as Mr. Justice Holmes put it, 'of

preventing people from getting other people's property for nothing when they purport to be buying it.") (quoting *Continental Wall Paper Co. v. Louis Voight & Sons Co.*, 212 U.S. 227, 271 (Holmes, J., dissenting)).

The foregoing applies at a minimum to all existing licenses. Were this Court to reverse the Federal Circuit's bar on declaratory judgment actions by licensees in MedImmune's position, the effects on future licenses would also be harmful. Although the Solicitor General suggests that licensors may include enforceable provisions terminating licenses upon licensee suit, or establishing higher royalty rates upon prevailing in such a suit, there are two fundamental problems with the suggestions. First, even such provisions add to negotiations, thus delaying and increasing the costs of reaching any agreement. Second, the Solicitor General is unwilling to assert that such provisions actually would be enforceable. Without that certainty such provisions are no comfort. Prospective licensors would therefore have a strong incentive, or even be compelled, before entering into a license, to file suit against the potential licensee (perhaps with its consent) and propose the license as a settlement that would then have *res judicata* effect. The remedy of a declaratory judgment should not be made available to produce such waste of judicial and private resources.

Permitting declaratory judgment suits by licensees in good standing would also lead to "a deterioration in business ethics in the patent licensing marketplace." 7 PAT. L. PERSP. § 12.4[6], at 12-123. MedImmune's proposed standard would encourage licensees to enter into license agreements as a pre-litigation tactic affording a safe platform from which to litigate. Operating under the protection of the license, the licensee could then turn around and sue the licensor (who remains bound by the contract) at a time and often in a jurisdiction of the licensee's choosing.

This is not hypothetical – it is precisely the tactic used by MedImmune prior to filing the *Centocor* litigation. There is, accordingly, a real danger that other current and potential licensees will engage in similar conduct if MedImmune's tactics are rewarded by this Court.

Under settled declaratory judgment standards, the adverse consequences for licensors and the resulting danger to the public substantially outweigh the needs of a plaintiff licensee in good standing who is in no danger of being sued. MedImmune offers no valid, supportable principle for rejecting a standard that holds licensees to obligations they voluntarily undertook, while providing a prompt, pre-license (or post-breach) opportunity to litigate patent validity.

## CONCLUSION

The judgment should be affirmed.

Respectfully submitted.

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# APPENDIX

## APPENDIX A

## LIST OF AMICI CURIAE

### THE AMERICAN ASSOCIATION OF MEDICAL COLLEGES

The Association of American Medical Colleges ("AAMC"), founded in 1876, is a private voluntary non-profit association of medical schools, teaching hospitals, health systems, and academic societies. Its membership includes the nation's 126 accredited medical schools, nearly 400 teaching hospitals, and more than 105,000 faculty in 98 academic and scientific societies.

### THE ASSOCIATION OF AMERICAN UNIVERSITIES

The Association of American Universities ("AAU") is an organization of research universities devoted to maintaining a strong system of academic research and education. It consists of 60 U.S. universities and two Canadian universities, divided about evenly between public and private. Today, the primary purpose of the AAU is to provide a forum for the development and implementation of institutional and national policies promoting strong programs in academic research and scholarship and undergraduate, graduate, and professional education.

### THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY

The Board of Trustees of the Leland Stanford Junior University ("Stanford") is one of a select group of universities that has achieved eminence in both undergraduate and graduate education in a broad range of

academic disciplines. Stanford has more than 6,700 undergraduate students, nearly 8,200 graduate students and nearly 1,800 faculty members. The accomplishments of Stanford faculty member include 15 Nobel laureates, 3 National Medal of Technology recipients, 134 members of the National Academy of Sciences and 82 National Academy of Engineering members. Stanford's Office of Technology Licensing, which is responsible for the issuance of more than 1,500 patents, is guided by the principle of "doing what is best for the technology" which routinely results in licensing for the public benefit.

## THE CALIFORNIA INSTITUTE OF TECHNOLOGY

The California Institute of Technology (Caltech) is one of the world's major research centers with an outstanding faculty, including five Nobel Laureates, and a student body of approximately 900 undergraduates and 1000 graduate students in science and engineering. Caltech is consistently among the top three universities that receive United States patents, which it licenses to benefit the public and to fund research.

## THE COUNCIL ON GOVERNMENTAL RELATIONS

The Council on Governmental Relations ("COGR") is an association of more than 170 U.S. research universities and their affiliated academic medical centers and research institutes. COGR concerns itself with the influence of government regulations, policies, and practices on the performance of research conducted at its member institutions. COGR has a longstanding interest in and concern for assuring the continued effectiveness of the Bayh-Dole Act (P.L. 96-517) and implementing federal regulations (37

C.F.R. 401 et. seq.) in facilitating technology transfer by U.S. universities.

## THE NATIONAL ASSOCIATION OF STATE UNIVERSITIES AND LAND-GRANT COLLEGES

The National Association of State Universities and Land-Grant Colleges ("NASULGC") was founded in 1887 and is the nation's oldest higher education association. Its members include public universities, public-university systems, and land-grant institutions from all 50 states, the U.S. territories and the District of Columbia. Many of the top 100 recipients of federal funds for research and development are NASULGC-affiliated institutions.

Much research performed by universities affiliated with NASULGC is directed to core issues at the forefront of basic science. Groundbreaking university research is later developed - through substantial investment by licensees - into products with wide public benefit. NASULGC and its members have an interest in assuring that universities should not be disadvantaged in their patent rights.

## THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

The Regents of the University of California is a public university of ten campuses and five medical schools together with two national laboratories operated by The Regents on behalf of the U.S. Department of Energy. The Regents provide for technology transfer for each site as a part its mission of education, research and public service.

## THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

The Trustees of Columbia University in the City of New York ("Columbia") is a private, nonprofit institution of higher education whose activities are concentrated at two locations in New York City and extend around the globe. Columbia provides instruction through 16 undergraduate, graduate, and professional schools, including one of the largest academic medical centers in the United States, and conducts research, training, and other services under grants and contracts with agencies of the federal government and other sponsoring organizations. Columbia enrolls approximately 23,800 students and employs approximately 12,600 full-time employees, including 4,700 full-time faculty members.

## THE UNIVERSITY OF WASHINGTON

The University of Washington is a public research university with campuses in Seattle, Bothell, and Tacoma. It has over 27,600 faculty and staff, and almost 43,000 students. Annually, the University receives almost $1.0 billion in sponsored research support from federal, foundation, and industrial sources.